Right Ventricular diastolic function assessment by tissue Doppler in Mitral Stenosis—Correlation with functional capacity.

A DISSERTATION
SUBMITTED IN PARTIAL FULFILLMENT
OF DM – BRANCH II CARDIOLOGY EXAMINATION
OF THE DR. MGR UNIVERSITY, CHENNAI.
TAMILNADU.
TO BE HELD IN JULY/AUG 2008.

CERTIFICATE

This is to certify that the thesis titled **"Right Ventricular diastolic function assessment by tissue Doppler in Mitral Stenosis—Correlation with functional capacity"** is the bonafide work of **Dr.Sanjeev Salilkumar Mukherjee** towards the DM - Branch II (Cardiology) Examination of the Tamilnadu Dr. MGR Medical University, Chennai, to be conducted in July / August 2008.

Dr. George Joseph, MD DM(CARD)
Professor& Head,
Department of Cardiology,
Christian Medical College,
Vellore – 632 004.

CERTIFICATE

This is to certify that the thesis titled **"Right Ventricular diastolic function assessment by tissue Doppler in Mitral Stenosis—Correlation with functional capacity"** is the bonafide work of **Dr.Sanjeev Salilkumar Mukherjee** towards the DM - Branch II (Cardiology) Examination of the Tamilnadu Dr. MGR Medical University, Chennai, to be conducted in July / August 2008.

Guides:

Dr. Paul V George, MD DM(CARD)
Professor & Ag. Head
Department of Cardiology Unit II,
Christian Medical College,
Vellore – 632 004.

Dr. V. Jacob Jose, MD DM(CARD) FACC, MS, FCCP, FIAE
Professor
Department of Cardiology,
Christian Medical College,
Vellore – 632 004.

ACKNOWLEDGEMENTS

I am deeply indebted to my teacher, Dr.V. Jacob Jose, Professor of Cardiology, who gave me the idea and provided me invaluable advice and guidance throughout the study.

I am grateful to, Dr.George Joseph, Head of the department, Cardiology, and Dr.Sunil Chandy, Professor of Cardiology, for allowing me to recruit patients from their respective units. I would like to thank Dr.Paul V. George,Professor of cardiology for correcting the manuscript and for all the help rendered.

I thank, Mr.Solomon, Department of Biostatistics for helping me in analysis of the data. I acknowledge the help of Sasikala PK, Wales Paul and my colleagues who helped me in different ways for the completion of study. At the end I must thank all my patients for their co-operation.

Dr.Sanjeev Mukherjee

CONTENTS

			Page
1.	INTRODUCTION	…	1
2.	AIMS AND OBJECTIVES	…	3
3.	REVIEW OF LITERATURE	…	4
4.	MATERIALS AND METHODS	…	50
5.	RESULTS	…	55
6.	DISCUSSION	…	63
7.	LIMITATIONS	…	66
8.	CONCLUSION	…	67
9	BIBLIOGRAPHY	…	68
10.	APPENDIX –PROFORMA	…	80
11.	MASTER DATA SHEET		
12.	GLOSSARY FOR MASTER DATA SHEET	…	82

Right Ventricular diastolic function assessment by tissue Doppler in Mitral Stenosis—Correlation with functional capacity.

INTRODUCTION

Rheumatic heart disease still remains a major cause of morbidity and mortality in developing nations with recent reports suggesting approximately 15 million cases in these countries (1,2). The above figure may underestimate the actual burden of this disease as these estimates are based on prevalence data obtained by comprehensive clinical screening rather than echocardiographic screening which might detect approximately 10 times as many cases in South East Asia and Sub-saharan Africa(3).

Mitral stenosis (MS) due to rheumatic heart disease is associated with considerable fusion of commissures and reduction of mitral valve apparatus and leaflet mobility (4,5). Although symptoms of dyspnoea and fatigue are common in patients with mitral stenosis, mechanisms that limit exercise tolerance are poorly understood (6). It is well known that determination of functional capacity in cardiovascular disease is very essential for the evaluation of response to treatment, prognosis and timing of invasive procedures (7). In isolated mitral stenosis invasive procedures are recommended for symptomatic patients with valvular area of less than or equal to 1.5cm² according to ACC/AHA guidelines (8). Intervention in mitral stenosis is generally indicated when symptoms occur or when pulmonary hypertension develops (9). Therefore, whether patient is symptomatic or not is important. Increasing mitral valve obstruction leads to progressive elevation in capillary and pulmonary artery pressure (PAP) and augmented symptoms. Therefore, identification of the determinants of PAP in mitral stenosis is clinically important. Risk of right ventricular dysfunction always exists due to reactive vascular changes in pulmonary arteries and rheumatic myocardial

involvement in mitral stenosis. At times termed "the forgotten ventricle," (10) the right ventricle plays an important role in clinical presentation in mitral stenosis and many such cardiac pathologies. The right ventricular systolic function is an important determinant of clinical symptoms, exercise capacity, pre operative survival and post operative outcomes in patients with mitral stenosis (11). There has been lot of studies which showed the importance of right ventricular systolic function in mitral stenosis, but very limited data cocncentrating on diastolic function . In the present study we tried to assess right ventricular diastolic function and Tei Index and compared them between asymptomatic and symptomatic patients with moderate to severe mitral stenosis.

AIMS AND OBJECTIVES

1. To assess the incidence of right ventricular diastolic dysfunction in asymptomatic and symptomatic patients with moderate to severe rheumatic mitral stenosis

2. To assess the relation between symptomatic and asymptomatic rheumatic mitral stenosis patients and right ventricular Tei index as calculated by colour tissue Doppler.

REVIEW OF LITERATURE

Introduction :

Although the attack rate for rheumatic fever is roughly equal among genders, mitral stenosis (MS) is 2 to 3 times more common in women. It is generally believed that the M protein antigen held in common between the heart and group A hemolytic Streptococcus results in an autoimmune attack of the heart in response to streptococcal infection(12–14). What factors cause susceptibility to the illness remain unclear. Likewise, factors responsible for the decline in MS incidence in developed countries are also obscure. Although the decline may be due in part to the introduction of antibiotics, a fall in the attack rate of rheumatic fever began well before antibiotics were widely available (15). Once begun, the rheumatic process leads to inflammation in all 3 layers of the heart: endocardium, myocardium, and pericardium. However, the disease primarily affects the endocardium, leading to inflammation and scarring of the cardiac valves. Although the process is punctuated by acute episodes of rheumatic fever, chronic inflammation and scarring continue well after the last attack, leading to severe valve damage years later. The mechanism of this chronic process is debatable and is thought to be due either to a continuing low-grade rheumatic process or to hemodynamic stresses on the now-injured valve. Elevated C-reactive protein levels, indicative of ongoing generalized inflammation, are found in many patients before balloon mitral valvotomy, which supports an inflammatory origin for MS (16). Although all of the cardiac valves may be involved by the rheumatic process, the mitral valve is involved most prominently and in virtually all cases. Stenosis of the mitral valve occurs from leaflet thickening, commissural fusion, and chordal shortening and fusion.

Occasionally, mitral annular calcification rather than disease of the valve leaflets and chordae tendineae is the cause of mitral stenosis. Other exceedingly rare causes of MS include use of anorectic drugs and carcinoid syndrome (17).

Epidemiology:

The epidemiology of acute rheumatic fever (ARF) is linked with that of Group A beta-haemolytic streptococcal pharyngitis; both have a maximum incidence in the age group of 5 - 15 years(18). In developed countries, ARF/rheumatic heart disease (RHD) have become uncommon health problems during the past two decades. In contrast, in third world countries such as India, the middle-east, sub-Saharan Africa, ARF remains the leading cause of heart disease in children and young adults (19). According to the WHO, at least 15.6 million people have RHD. Of the 5,00,000 individuals who acquire ARF every year, 3,00,000 go on to develop RHD; and 2,33,000 deaths annually are attributable to ARF or RHD (20). However, these estimates are based on conservative assumptions, so the true burden of the disease is likely to be substantially higher. The prevalence of ARF/RHD in India has been reported to be varying from very infrequent to very high levels depending upon the source of information e.g., Registrar General, population sources, and hospital admissions. Recent data from India suggest that a large number of cases of ARF/RHD are still seen frequently in young children under the age of 10 years. From Delhi, Sharma *et al* examined 191 children below 12 years of age with definitive clinical features of ARF (21). As regards the age group, 60% children were between 9 - 12 years, 31.4% were between 5 - 9 years and only 7.9% were below

5 years. A study from Orissa reported a prevalence of RHD in 378 children below 19 years (mean age 15.1 ± 4.4 years) as mild mitral stenosis (MS) in 34.9% and severe MS in 33% with a 4:1 male : female ratio (22). The prevalence of ARF in school children of Kanpur District in Uttar Pradesh was 0.75/1,000 (rural 1.20 and urban 0.42) (23). The largest school survey conducted to date in India at our institute in Vellore during 2001 - 2002, a total of 2,29,829 children between 6 - 18 years of age were screened as part of a school health programme. Dr.Jose et al. (24) reported that the prevalence of RHD was 0.68/1,000 school children, showing a declining prevalence of RHD in rural children in southern India.

In contrast, there are studies from other parts which have reported no significant decline in prevalence of ARF/RHD in India (25). In one study from Eastern India done between 1981 - 1990, showed that 9.2% of admitted cases had ARF, whereas during the period 1991 - 2000, 8.9% of admitted cases had ARF. Thus, there was marginal decline in prevalence of ARF which was not statistically significant. During the epidemic of streptococcal pharyngitis, the primary attack rate is around 3%. Streptococcal pharyngeal infection in patients with history of recent ARF may produce a secondary attack rate of as high as 65% (26). In the Irvington House Study, rheumatic attack rate per infection (R/I) in children decreased from 23% to 11% between the first and fifth year after the last attack (27).

In India, the average age of presentation of ARF is between 10 to 14 years (28). First episodes of ARF are most common just before adolescence, wane by the end of the second decade, and are rare in adults older than 35 years (29). RHD usually results from cumulative damage of recurrent episodes of ARF, although initial attacks can

directly lead to RHD. The prevalence of RHD increased with age, peaking in adults aged 25 - 34 years reflecting ARF activity in previous decades.

Pathogenesis:

Although the pathogenesis of ARF and RHD remains somewhat elusive, ARF is clearly the result of an exaggerated immune response to specific bacterial epitopes in a susceptible host (1). The association between Group A beta-haemolytic streptococci, upper respiratory tract infection and the subsequent development of ARF is fairly well established. The exact pathogenetic mechanisms are unknown largely due to lack of an animal model. Two basic mechanisms are implicated:

(1) A toxic effect of the extra-cellular Group A beta-haemolytic streptococci on target organs like myocardium, valves, synovium, and brain

(2) An abnormal immune response of host to the streptococcal antigen (17). Some strains of Group A streptococcus are more likely to cause ARF, i.e., M types 1,3,5,6,14,18,19,and 24.

However, some have challenged this theory, arguing instead that rheumatogenicity is not restricted to organisms belonging to only a few serotypes (29). Classically, rheumatogenic M serotypes are infrequently found in several communities with high burdens of ARF and RHD, where newly identified serotypes have been linked with disease (30). The autoimmune response that causes ARF is triggered by molecular mimicry between epitopes on pathogen (Group A streptococci) and specific human tissues. The structural and immunological similarities between streptococcal M protein

and myosin – both alpha-helical, coiled coil molecules – seem essential to the development of rheumatic carditis (29). However, valvular disease, rather than acute myocarditis, is responsible for most of the cardiac morbidity and mortality of ARF. There is evidence that antibodies to cardiac valve tissues cross – react with N-acetyl glucosamine in group A carbohydrate (31). An exaggerated antibody response to group A carbohydrate has been detected in patients with ARF, and titres remain raised in individuals with residual mitral valve disease, providing further support to the concept that these antibodies cause valve damage.

The Host :

In spite of knowledge about the inciting agent, it is not well understood why only certain individuals develop ARF subsequent to streptococcal pharyngitis. The immunological system of the host including both cell-mediated and humoral is an important factor for the susceptibility to ARF, but the exact mechanisms are unknown (18). Certain genetic influences also seem to play a role since only about 3% of individuals develop ARF following acute streptococcal pharyngitis. There is also higher concordance among monozygotic twins for development of ARF. A B-lymphocyte alloantigen has been implicated in the determination of susceptibility to ARF in 70 - 90% of rheumatic patients (32) HLA types, viz., HLA-DR 1, 2, 3, and 4 haplotypes have also been implicated in certain ethnic groups.

Pathologic Evolution of Mitral Stenosis:

During acute rheumatic fever with carditis, involvement of the mitral valve consists of tiny, translucent nodules located along the line of closure of the valve, occasionally also involving subvalvular parts of the chordae. Aschoff bodies are not usually encountered upon the valve tissue. Microscopic sections of these nodules show largely nonspecific proliferation of fibroblasts and macrophages. These translucent vegetations later become opaque and gray, and eventually more of the valve leaflet becomes thickened. Changes within the valve structure involve deposition of fibrin upon the cusps with loss of the normal morphology, hyalinization, and eventually the covering of the leaflets with endothelium. This process may lead to fusion of the valve

commissures. Brock (33) postulated that the initial point of fusion of the two leaflets occurred at the "critical area of tendon insertion," i.e., the point where the shortest and most direct chordae connect with the cusps. When fusion occurs at these points, portions of the cusps lateral to them are immobilized, thereby facilitating more commissural fusion. When mitral stenosis is fully developed, three distinct types have been recognized: (34)

1. commissural type, consisting of fusion of the commissures with little involvement of cusps or chordae;
2. cuspal type in which the leaflets are converted into stiff, rigid, leathery (later calcified) structures; and
3. chordal type in which the chordae are fused, thickened, and shortened, thereby interfering with the mobility of the leaflets. In addition to the pure forms, combinations of these types occur.

The various anatomic forms of mitral stenosis may affect atrioventricular filling in similar manner. The degree of mitral valve obstruction is often fixed, due to commissural fusion, and possibly, to the chordal abnormalities (fig. 1B). However, in the pure cuspal form (fig. IC) of mitral stenosis, the degree of apparent valve narrowing, as evidenced clinically and hemodynamically, appears more severe than that found anatomically. This physiologic-anatomic dissociation is likely related to stiffened and possibly calcified valve cusps; these cusps, while potentially mobile, may fail to open in response to a given left atrial pressure, regardless of whether the commissures are fused or not. It is

therefore possible to have the mitral valve "wide open" on surgical or pathologic inspection, and yet to have the valve remain severely stenotic under in vivo conditions.

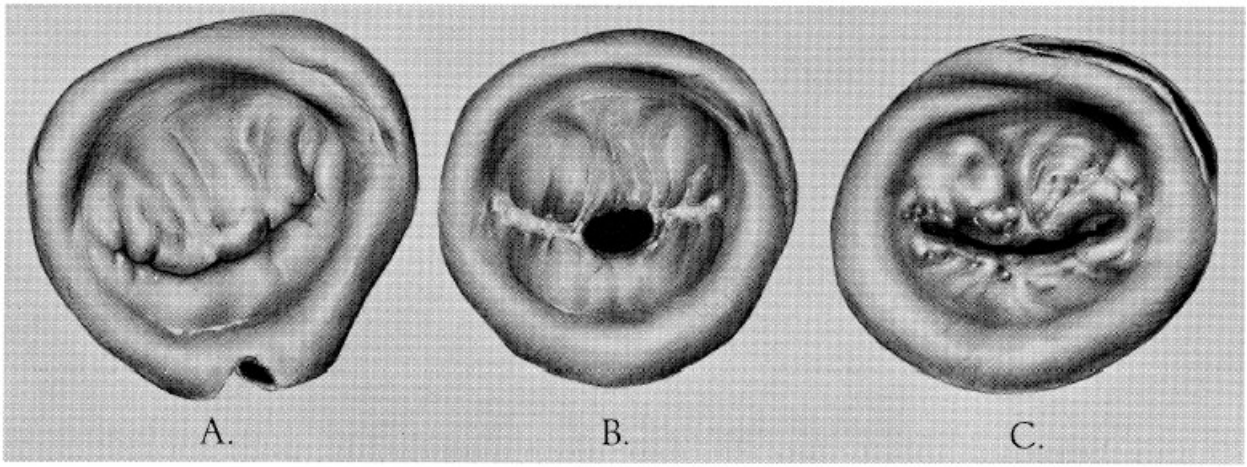

Fig 1:Drawing of three mitral valves: (A) Normal mitral valve in a closed position, viewed from the atrium. (B.) Stenotic mitral valve with commissural type of stenosis, showing maximum opening; commissural fusion joins leaflets of normal thickness and mobility. (C.) Cuspal type of mitral stenosis: only minimal fusion of commissures is present, but the stiff, fibrocalcific leaflets cannot open under- physiologic pressure.(Reproduced from Circ.1972:XLV:884)

Pathophysiology of Mitral Stenosis:

The normal mitral valve orifice is 4 to 5 sq. cm., which essentially creates a common chamber between left atrium and left ventricle in diastole. In very early diastole, there is a brief, small gradient between left atrium and left ventricle, which rapidly dissipates (Figure 2A) so that pressure in the 2 chambers is equal for most of the filling. As the mitral orifice narrows in MS, it curtails free flow of blood from left atrium to left ventricle, and a pressure gradient develops between the 2 chambers (Figure 2B).

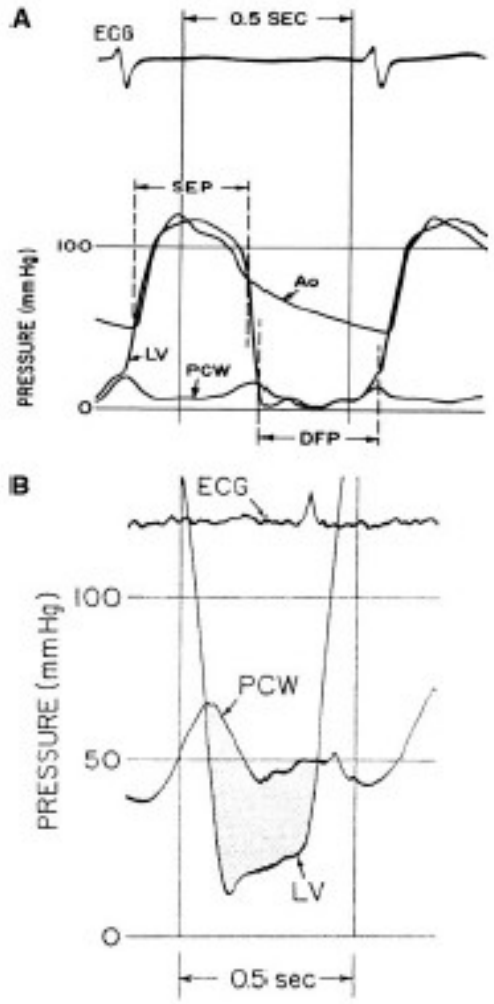

Figure 2A
A, Normal left ventricular (LV), left atrial, and aortic
(Ao) pressure tracings are shown. DFP indicates diastolic filling period; SEP, systolic ejection period.

Figure 2B, Pressure gradient between pulmonary capillary wedge pressure (PCW) and left ventricle (LV) is shown for patient with MS. In this figure, left ventricular end-diastolic pressure is atypically elevated, consistent with coincident mitral regurgitation.

Ref : Reproduced from Circulation 2005;112:433)

This pressure gradient is added on to left ventricular diastolic pressure, which results in increasing left atrial pressure that eventually leads to left atrial enlargement and pulmonary congestion. As stenosis severity worsens, flow restriction limits left ventricular output. Pulmonary congestion and reduced cardiac output mimic left ventricular failure. Although it is generally believed that left ventricular contractility is normal in most cases of MS, the issue of a “myocardial factor,” ie, left ventricular damage caused by rheumatic fever, has often been raised without unanimity. Although ejection phase indexes of left ventricular function are reduced in approximately one third

of patients with MS, decreased preload from impaired filling and increased afterload secondary to reflex vasoconstriction (secondary to reduced cardiac output) are usually the causes of reduced left ventricular function rather than impaired contractility. However, in this subcontinent where rheumatic inflammation appears to be very aggressive, true contractile impairment may be present.

Because it is primarily the right ventricle that generates the force necessary to drive blood across the stenotic mitral valve, MS causes right ventricular pressure overload. In severe MS, pulmonary vasoconstriction in addition to left atrial hypertension produces severe pulmonary hypertension, which leads to right heart failure. Thus it is essential to understand the importance of right ventricular function and methods to assess it.

Right Ventricular Function

The results of an electronic search of the literature of the last three decades underscore the lack of attention paid to right ventricular form and function, publications concerning the left ventricle outnumber those of the right ventricle by approximately 10 to 1 (Fig. 3).

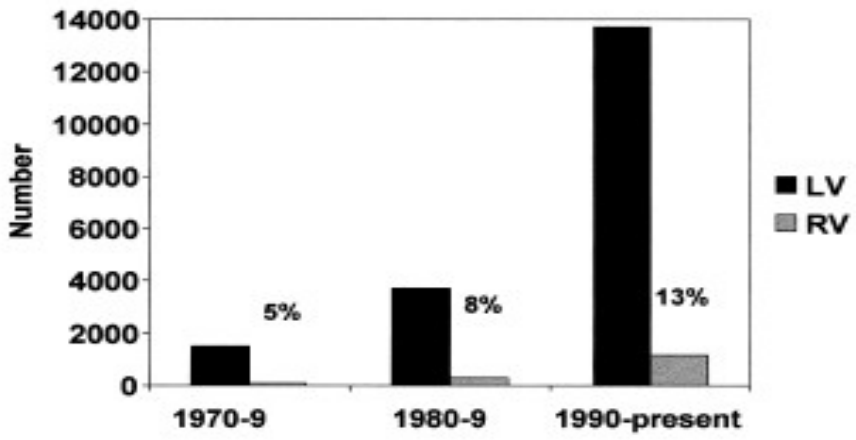

Fig 3: A bar-chart showing number of publications regarding right (RV) and left ventricular (LV) function.(Reproduced from Cardiology Clinic 2002;20:342)

Nonetheless, the last decade has seen increased recognition of the importance of right ventricular function in the circulation. The negative impact of coexisting right ventricular dysfunction in dilated & ischemic cardiomyopathy and valvular heart disease is well established, for example [35], but it is in congenital heart disease where right ventricular dysfunction is now accepted as being pivotal to the natural and unnatural history of so many of the disease complexes. While ignorance of the potential impact of dysfunction may explain some of the lack of attention paid to the right ventricle, there is another pragmatic, but no less important, reason for the relative scarcity of mechanistic research. There can be no doubt that the adequate assessment of right ventricular performance is more difficult than that of its left ventricular counterpart. While the prolate ellipsoid of the left ventricle lends itself to geometric assumptions and mathematical interpretation, the shape, geometry, and anatomical location of the right ventricle all conspire against precise assessment. Add to this the effects of coexisting congenital abnormalities, beat to beat changes occurring with respiration, the profound changes that may occur with abnormalities of the pulmonary vascular bed, and right/left

heart interactions, and it is easy to see why understanding of right ventricular function has lagged behind that of the left. Nonetheless, each of these issues is of fundamental importance to the physiology of the circulation as a whole, and a variety of methods are now available for the assessment of right ventricular performance.

Right Ventricular Physiology

With the exception of small physiologic shunts, the average cardiac output from the right ventricle must, of course, be the same as the cardiac output from the left ventricle. The mechanism by which right ventricular stroke output is achieved, is very different from that of the left. This is almost entirely a consequence of the very different vascular beds into which the right and left ventricles empty.

Energetically, the external work performed by the right ventricle to generate the cardiac output is approximately one quarter to one fifth of that expended by the left ventricle. This is illustrated perfectly by analysis of right and left ventricular pressure volume relations (Fig. 4A) The left ventricle is essentially a square wave pump, and its external stroke work can therefore be approximated to the stroke volume multiplied by the diastolic to systolic pressure difference [36]. While the left ventricular pressure volume diagram was elucidated in the 1960s [37], it was not until the 1980s, that the pressure-volume relationship of the normal right ventricle was described [38]. Earlier observations by Shaver and coworkers [39], examining simultaneous micro-manometer pressure recordings from the right ventricle and pulmonary artery, suggested that the

normal right ventricle might operate under an entirely different set of pressure volume conditions to that of the left ventricle. The ‘‘hang out’’ period between the onset of right ventricular pressure decline, and the dicrotic notch of pulmonary valve closure suggested that right ventricular ejection was occurring well beyond the development of peak right ventricular pressure. This was confirmed by direct analysis of right ventricular pressure volume relationships constructed using a bi-plane angiographic method to measure right ventricular volume combined with micromanometer-tipped pressure catheter recordings [38]. Fig. 4B shows a typical example. Compared with the normal left ventricle, ejection from the right ventricle occurs early during pressure rise (with an abbreviated period of isovolumic contraction) and continues as right ventricular pressure declines. Thus, the normal right ventricular pressure volume relationship is more trapezoidal or triangular, and the external mechanical work (the area subtended by the loop) proportionately smaller then that of a square wave pump with similar stroke volume and peak developed pressure. This capacity to eject during pressure rise and decline is mechanically very efficient, but crucially dependent on the low hydraulic impedance imposed by the normal pulmonary vascular bed. Relatively subtle changes in right ventricular afterload can result in large changes in this energetic efficiency. Increased pulmonary vascular resistance promptly alters the shape of the right ventricular pressure volume relationship to something more akin to that of the left [40]. In conditions such as pulmonary stenosis, or when the right ventricle is the systemic ventricle, the pressure-volume characteristics may be indistinguishable from a normal left ventricle. It should be remembered, however, that while there is a large contractile reserve when its afterload is increased slowly (i.e. over weeks or months), the right

ventricle is much more prone to acute failure with relatively

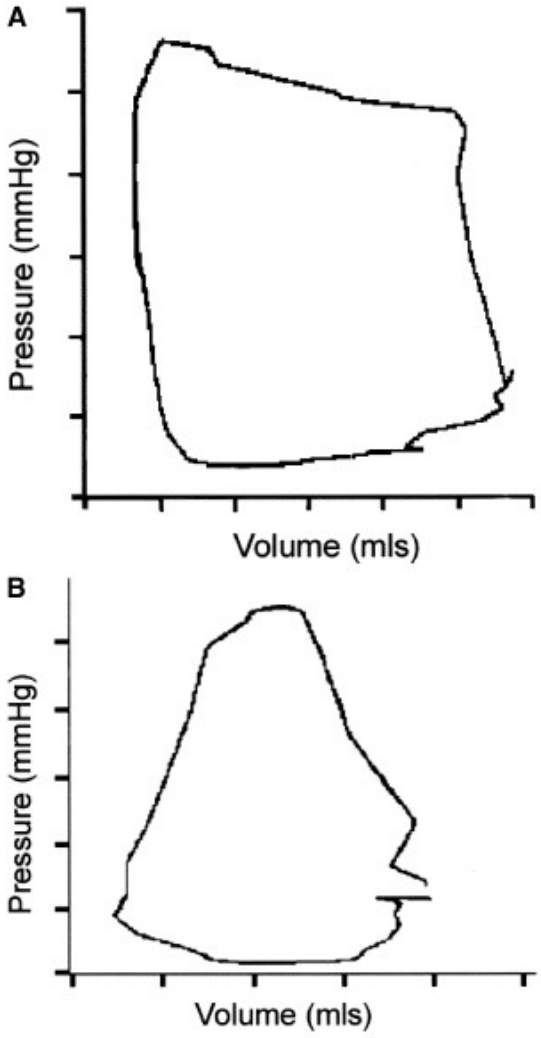

Fig.4: (A) A normal left ventricular pressure-volume loop
(B) A pressure-volume loop from the normal right ventricle
(Reproduced from Cardiology Clinic 2002;20:342)

modest increases in afterload. Indeed, the afterload sensitivity of the right ventricle is 2 or 3 times that of left ventricle(41).

Consequently, there is an almost linear inverse relationship between right ventricular ejection fraction and right ventricular afterload [42]. It should be clear therefore that the application of concepts derived from the understanding of left ventricular contractile physiology need not necessarily apply directly to that of the right. Similarly, the diastolic properties of the right ventricle are very different from those of the

left ventricle. Interestingly, while the diastolic phase of right ventricular filling, as assessed from the pressure volume relationship, may remain stable even with relatively large changes in afterload, it is markedly pre-load dependant. For example, the pressure volume trajectory in response to an acute volume load is much steeper in the right ventricle compared to the left, suggesting greater inherent myocardial stiffness or reduced chamber compliance. Paradoxically, the right ventricle adapts more readily to a chronically increased pre-load. Gross right ventricular dilation (of a greater degree, and tolerated for much longer than would be possible by the left ventricle) can occur with little or no apparent change in basal compliance characteristics. That is, despite a doubling or tripling of right ventricular end diastolic volume, there may be little or no change in right ventricular end diastolic pressure. It must be remembered however that, unlike the left ventricle, the right ventricle is not necessarily a closed system in diastole. The high aortic diastolic pressure maintains aortic valve closure throughout diastole, even in the presence of a markedly raised left ventricular end-diastolic pressure. The low pulmonary artery end-diastolic pressure associated with a low pulmonary vascular resistance is easily exceeded by right atrial systolic pressure under some circumstances. As a result, real changes in myocardial compliance may not be reflected by changes in either ventricular pressure, volume or pressure-volume characteristics. As will be discussed later, restrictive right ventricular physiology may therefore be associated with normal trans-tricuspid flow characteristics, normal right ventricular end-diastolic pressure and volume, and normal right ventricular pressure volume relations, despite markedly abnormal right ventricular myocardial properties [43]. So far, the differences between right and left ventricular physiology have been described as if the

two ventricles were separate entities. While this is convenient, it is physiologically inappropriate. Left and right ventricular systolic and diastolic ventricular performance is affected by phenomena occurring on the contralateral side of the heart. These right-left heart interactions are amplified by the effect of disease, but are present in all of us as part of normal ventricular physiology.

Right ventricular–left ventricular interaction :

While the deeper layers of myocardial fibers are separated, there are shared superficial fibers that encircle the normal left and right ventricle. Furthermore, in some forms of congenital heart disease the deeper layers of the right and left ventricle may be contiguous within the interventricular septum (44). The function of the two ventricles is therefore inextricably linked, in both the structurally normal and abnormal heart. The potential for left to right ventricular myocardial ‘‘cross-talk’’ was beautifully demonstrated in an experimental study of intact explanted hearts in which electrical, but not mechanical, continuity between the right and left ventricles had been interrupted [45]. Pacing the right ventricular myocardium led to little detectable mechanical activity (measured as developed pressure) in the left ventricle. Conversely however, pacing-induced contraction of the electrically isolated left ventricle was associated with the development of an almost normal right ventricular pressure trace [43]. Indeed, it was estimated that over 50% of the mechanical work of the right ventricle, may be generated by left ventricular contraction. Hoffman and coworkers shed more light on this

phenomenon in a series of in vivo experiments [46]. By replacing the right ventricular myocardium with a non-contractile prosthesis, they were able to show virtually normal right ventricular pressure generation, as a consequence of normal left ventricular shortening. Just as interesting, was the observation that intact right ventricular geometry is crucial for normal left ventricular mechanical performance. During gradual enlargement of the non-contractile right ventricular free wall, there was a progressive reduction in both right ventricular mechanical work, but also left ventricular mechanical work, i.e. as the right ventricle dilated, left ventricular pressure development and stroke work fell. This simple observation may have huge implications for our understanding and management of left ventricular dysfunction in the presence of the chronic right heart disease (and vice-versa) in congenital and acquired defects.

All of these effects are amplified by the superimposition of pericardial constraint. While chronically the pericardium usually has the capacity to enlarge commensurate with the size of the ventricular mass, this cannot occur acutely. Just as an acute pericardial effusion can impose major, life threatening, hemodynamic abnormalities, the rapid dilation of a cardiac chamber can have similar effects. Brookes et al examined the effects of acute right ventricular dilation (imposed by selective right coronary ischemia) on both right and left ventricular performance measured by conductance catheter [47]. With an intact pericardium, acute right ventricular dilation led, unsurprisingly, to a commensurate reduction in left ventricular size, and load-independent indices of contractility. This effect was mediated primarily by septal shift. This change in left ventricular volume was obviated by release of the pericardium. A similar degree of right ventricular dilation occurred, but there was a non-significant fall in left ventricular

volume.

Going along with Hoffman's observations [46] however, acute right ventricular dilation under these circumstances was also associated with a significant fall in load-independent measures of left ventricular myocardial contractility. This could not be explained on the basis of changes in left ventricular geometry, and almost certainly reflected abnormalities of myocardial cross talk under the circumstances of acute right heart dilation.

Cardio-pulmonary interactions:

The importance of the relationship between right and left heart function, described above, is matched by a similarly intimate relationship between the right heart and the lungs. The effect of cyclical changes in venous return on right heart hemodynamics has already been discussed, and will be further emphasized throughout this chapter. This cardio-venous relationship is just one of the manifestations of cardio-pulmonary interaction. Changes within the lungs themselves as a result of the mechanical work of breathing, changes in pulmonary vascular resistance (with the secondary effects on right ventricular contractile physiology described earlier), and intra-thoracic pressure can all be equally important in both the ambulatory patient and, in particular, the patient requiring positive pressure ventilation. Normal inspiration supplies work to the circulation. It has been estimated that approximately 30% of pulmonary blood flow (and therefore cardiac output) in Fontan circulation can be directly attributed

to this inspiratory work [48]. This cardio pulmonary adaptation is manifest also on exercise. The adverse effects of positive pressure ventilation are also most marked in patients lacking a sub-pulmonary right ventricle. There is essentially a linear inverse relationship between mean airway pressure and pulmonary blood flow [49,50]. As mean airway pressure rises (because of the imposition of positive end expiratory pressure, the use of prolonged inspiratory or plateau times, or auto-PEEP) the cardiac output will fall. The perioperative management of these patients should therefore be to establish normal respiration as soon as possible, and in those requiring positive pressure ventilation, to minimize the mean airway pressure, while maintaining adequate ventilation and small airway patency. All of these effects are seen in the bi-ventricular circulation, effected by right ventricular disease [43,50,51]. As mentioned earlier, systolic function of the right ventricle is exquisitely dependent on load. Even relatively small changes in mean airway pressure can significantly increase the afterload on the failing right ventricle.

In general, static imaging techniques measuring ventricular volume and its derivatives will fail adequately to describe either right ventricular systolic or diastolic performance, and therefore be consistently unable to predict the need for intervention. Ideally, dynamic assessment of load independent, as well as these load dependant, phenomena will be required. None of the individual techniques described below can therefore be considered to provide a comprehensive evaluation. Used together however, many of the questions asked of right ventricular performance can now be addressed, if not yet answered definitively.

Relevance of Right Ventricular Function :

The right ventricle is a structurally and functionally complex chamber whose importance has been neglected previously. It propels systemic venous blood returning from the right atrium through the pulmonary vascular bed and maintains haemodynamic stability. In clinical practice right ventricular dysfunction is relevant in a variety of conditions but for our study we will mainly concentrate on pulmonary vascular and mitral valve disease.

Pulmonary Vascular Disease:

In primary pulmonary hypertension the clinical features and mortality reflect the associated cardiac dysfunction manifest by progressive right ventricular pressure overload with hypertrophy and chamber dilatation. In the National Prospective Registry, pulmonary artery pressure, right atrial pressure and cardiac index measured at baseline were the best predictors of mortality confirming the important role of right ventricular performance in prognostic assessment (52). The vasodilator prostacyclin improves echocardiographic indices of right ventricular function which correlate with the improvement in quality of life and survival (53).

Mitral Valve Disease :

The importance of the right ventricle even in peri-operative morbidity and mortality in cases of valvular heart disease has been recognized several years ago. Thus, the right ventricle plays an important role not only for survival but also for the postoperative course and functional recovery of the patient with valve disease of the left heart (11).

Generally, the prognosis of patients with mitral valve disease and depressed right ventricular function improves significantly after successful intervention. However, according to Pinzani *et al.* (54) in the presence of right ventricular failure, mortality increases peri-operatively from 5 to 11% ($p<0.02$) and, during follow-up, from 8 to 22%

($p<0.0005$). Hirata *et al* (55) reported, in patients with a pre-operative right ventricular ejection fraction of less than 40%, no normalization of right ventricular ejection fraction after valve surgery. The persistence of symptoms after operation was higher in patients with a pre-operative right ventricular ejection fraction of less than 30% compared to those with a right ventricular ejection fraction of more than 30% (56). If right heart failure persisted after valve replacement, patients had a higher 5-year mortality (39%) than patients without right heart failure (4%; /$p<0.0001$) after surgery. A small number of patients developed right heart failure early after mitral valve surgery. These patients had a poor prognosis, with a mortality of 72% within 75 months of operation. The aetiology of perioperative right heart failure is multifactorial, and the pathophysiology is not yet fully understood. Groves and coworkers (57) reported a significantly lower exercise duration, a decreased maximal oxygen consumption and a lower anaerobic threshold in patients with than without tricuspid regurgitation late after successful mitral valve replacement. The presence of tricuspid insufficiency can explain the incomplete recovery from valvular surgery or the return of clinical symptoms in patients without prosthetic valve failure, persisting pulmonary hypertension or congestive heart failure.

Thus it becomes essential to assess right ventricular function prior to any mitral valve procedure. Till recently evaluating right ventricular function mainly needed magnetic resonance imaging (MRI) or radionuclide studies for exact evaluation. Comparative studies have proved it beyond doubt that right ventricular systolic function as assessed by tissue Doppler is comparative to other established modalities.

Assessment of right ventricular performance :

The importance of physical examination, the electrocardiogram, and in particular, the chest radiograph cannot be underestimated

Cardiac catheterization :

It would be an overstatement to suggest that cardiac catheterization is redundant in the clinical assessment of right heart disease, but invasive assessment of hemodynamics aside, the calculation of right ventricular volume using single plane and bi-plane geometric algorithms [38] has been consigned to medical history. At best, these techniques were time consuming and laborious, and many were conceptually flawed and inaccurate. For static measurements of right ventricular volume, magnetic resonance imaging is now unsurpassable. However, for dynamic right heart volume assessment, although remaining an experimental tool, conductance catheter assessment must now be the state of the art. The strength of the technique is its ability to measure beat by-beat changes in pressure-volume relationships acutely during interventions. Validated for right ventricular volume measurement (58,59), it has been used, for example, to quantify pulmonary regurgitant volume in response to simulated pulmonary artery stenosis in tetralogy of Fallot patients (60), and to assess right ventricular contractility using load independent end-systolic indices based on the elastance model of function (61). Indeed, it is only with such measurements that intrinsic myocardial dysfunction can be separated from the sometimes complex load-dependent

changes that are seen in adults. Clinically, diagnostic right heart catheterization is therefore reserved for the assessment of hemodynamics unmeasurable by other techniques (eg, right ventricular end-diastolic pressure, complex gradients, etc) or increasingly frequently, as a prelude to trans-catheter therapy of structural abnormalities which secondarily impose adverse effects on right ventricular performance.

Radionuclide studies :

Equilibrium and first pass radio-nuclide assessment of right ventricular volumes and ejection fraction have been used for many years. While the validity of such techniques has been established in the normal bi-ventricular heart, there are relatively few studies assessing their accuracy in the presence of intracardiac shunting, the anatomic and spatial abnormalities associated with congenital heart disease, and under the circumstances of important secondary hemodynamic phenomenon such as pulmonary or tricuspid incompetence. For these reasons, and the compelling data being achieved using the alternative techniques of echocardiography and magnetic resonance imaging, radio-nuclide studies are becoming a thing of the past.

Problems With Non-invasive Assessment of the Right Ventricle :

A number of factors contribute to the complexities of estimating right ventricular function. Whilst the left ventricular cavity approximates to an ellipsoid model in healthy individuals the right ventricle is considerably more complex. The main body of the chamber is crescentic and truncated with separate inflow and outflow portions. The outflow portion or infundibulum may account for up to 25% of the total right ventricular volume. The fact that the chamber poorly approximates to any convenient geometric model means that volume calculated with these models only crudely represents true volume (62-64). Marked regional differences exist in the extent of fibre shortening and contribution to stroke volume between different components of the right ventricle with

the contraction–relaxation sequence of the inflow portion preceding that of the infundibulum (65). The inaccessibility of the right ventricle behind the sternum often leads to inadequate image quality by conventional imaging modalities and this is particularly pertinent in patients with chronic pulmonary disease, a group in whom right ventricular dysfunction may be

present. In addition, the problem of accurately locating the endocardial boundary of the anterior wall of the chamber is compounded by a variable trabeculation pattern with the apical component having much coarser trabeculations than the corresponding zone of the left ventricle. Chamber orientation varies considerably between patients, particularly in those with right ventricular pressure or volume overload. In addition to myocardial function the shape and performance of the right ventricle depends on extrinsic factors such as pre-load, afterload and left ventricular performance. A limitation of conventional imaging methods in clinical practice is that these factors are frequently disregarded.

Echocardiographic evaluation of the right ventricle:

Due to its widespread availability, echocardiography is used as the first line imaging modality for assessment of right ventricular size and right ventricular function. The quantitative assessment of right ventricular size and function is often difficult, because of the complex anatomy. Nevertheless, when used in a qualitative fashion, two dimensional echocardiography can easily obtain valuable information about right ventricular size and function.

Two dimensional echocardiography:

For qualitative evaluation, the right ventricular size should be compared to the left ventricular size. In the parasternal long axis and apical four chamber views, the normal right ventricular is approximately two thirds the size of the left ventricle. If the right ventricle appears larger than the left ventricle and/or shares the apex, right ventricular dilatation may be present. Confirmation in other views is needed to avoid false positive findings. From short axis projections, the right ventricle should be smaller than the left while the left ventricular shape should have a circular geometry throughout the cardiac cycle. Finally, the right ventricle should also be evaluated from the subcostal projections. If the right ventricle appears larger in length or diameter, right ventricular dilatation is likely to be present . Right ventricular size (end systolic and end diastolic) and change in size during the cardiac cycle (right ventricular function) can also be quantitatively assessed by tracing the right ventricular endocardial border or measuring dimensions. However, this is often cumbersome and interobserver variability is high. Studies using endocardial tracing of the right ventricular area report relatively high correlations (0.69–0.88) between echocardiographically estimated right ventricular size and function compared to radionuclide angiography and MRI. However, the number of patients who could not be analyzed because of failure to trace the (entire) right ventricular myocardium is large (66); right ventricular tracing may be improved using intravenous contrast agents, that are commercially available. The most widely used quantitative technique is the area–length method in which a traced right ventricular lumen area in the four chamber view is combined with the right ventricular dimension in the parasternal short axis view. A different quantitative approach to assess right ventricular function is the measurement of the tricuspid annular plane systolic excursion

(TAPSE). The TAPSE estimates right ventricular systolic function by measuring the level of systolic excursion of the lateral tricuspid valve annulus towards the apex in the four chamber view. An excellent correlation between the TAPSE and subcostal projections without and with intravenous contrast injection has been found.

Right ventricular ejection fraction as assessed by radionuclide angiography appears reproducible and proved to be a strong predictor of prognosis in heart failure. The Doppler index of myocardial performance (Tei index or myocardial performance index) is yet another parameter that can be used for evaluation of right ventricular performance. It is expressed by the formula [(isovolumic contraction time + isovolumic relaxation time)/right ventricular ejection time]. It is established that this index is actually unaffected by heart rate, loading conditions or the presence and the severity of tricuspid regurgitation

There has been increasing recognition that diastolic ventricular function often plays an essential role in the clinical manifestations of disease in patients with a wide range of cardiac disorders. Diastolic dysfunction may be an early sign often antedating clinical or echocardiographic evidence of systolic dysfunction. In addition, the degree of diastolic dysfunction may explain the difference in clinical symptoms between patients with similar degrees of systolic dysfunction.

Phase of diastole:

The most widely accepted definition of diastole is the interval from aortic valve closure (end systole) to mitral valve closure (end diastole).

It is divided into four phases:

1. Isovolumic relaxation
2. Early rapid diastolic filling
3. Diastasis
4. Late diastolic filling due to atrial contraction

Echo assessment of RV diastolic dysfunction

The pattern of right ventricular diastolic filling is similar to left ventricular diastolic filling except that maximal velocities are lower (because the tricuspid annulus is larger) and the diastolic filling period is slightly shorter. Although few studies have addressed right ventricular diastolic filling, the same measurements described for left ventricular diastolic filling are applicable. Tissue Doppler can also be used to assess right ventricular wall velocities and diagnose diastolic dysfunction using similar criteria as used in left ventricle.

Doppler Data Recording :

On transthoracic echocardiography, right ventricular inflow can be recorded from the parasternal right ventricular inflow view or from the apical four-chamber view. Pulsed Doppler is used with the same technical considerations as apply to recording left ventricular inflow velocities. Evaluation of respiratory variation on inflow velocities is complicated by the respiratory motion of the heart, so care must be taken to ensure a parallel intercept angle between the ultrasound beam and inflow stream throughout the respiratory cycle. This can be accomplished in most patients by using a window where 2D echo showed little respiratory variation in the image plane itself or in the Doppler beam orientation relative to the 2D image. Tissue Doppler can also be used to assess right ventricular wall velocities and diagnose diastolic dysfunction using similar criteria as used in left ventricle.

Physiologic Factors That Affect Right Ventricular Filling

Right ventricular filling appears to be affected by all the same physiologic parameters that affect left ventricular filling, although less attention has been directed toward right ventricular inflow patterns. Again, the major differences between right ventricular and left ventricular filling are (1) timing, (2) reciprocal respiratory variation and (3) absolute velocities, which are lower for right ventricular inflow because the tricuspid annulus is larger than the mitral annulus.

Right Atrial Filling

Doppler velocity curves of right atrial filling can be recorded in the superior vena cava (from a suprasternal notch approach) or the central hepatic vein (from a subcostal approach), since these central veins empty directly into the right atrium without intervening venous valves. The pattern of right atrial filling recorded by Doppler parallels the jugular venous pressure curves seen clinically. However, the Doppler data represent a more reliable approach, since evaluation of jugular venous patterns is difficult in some patients due to body habitus and interpretation is subjective (with no recorded data).

Again, right atrial filling patterns show respiratory variation in normal individuals with augmentation of right atrial inflow during inspiration, as in seen in the right ventricular inflow pattern. A plausible explanation for these observations is that the negative intrathoracic pressure with voluntary inspiration (but not with mechanical ventilation) results in an extrathroacic to intrathoracic pressure gradient from the great veins into the right atrium, leading to increased blood flow into the right side of the heart.

Right atrial pressure can be estimated by echocardiographic evaluation (from the subcostal window) of the inferior venacava (IVC) as it enters the right atrium. The correlation with right atrial pressure is as mentioned below (67):

Estimation of Right Atrial Pressure

Inferior Vena Cava	**Change with Respiration or "Sniff"**	**Estimated Right Atrial Pressure (mmHg)**
Small (<1.5cm)	Collapse	0-5
Normal (1.5-2.5cm)	Decrease by > 50%	5-10
Normal	Decrease by < 50%	10-15
Dilated (>2.5cm)	Decrease < 50%	15-20
Dilated with dilated hepatic veins	No change	>20

Right atrial filling is most often evaluated from the subcostal window. After the long-axis view of inferior vena cava is obtained, the transducer is rotated and angulated to depict the central hepatic vein, which tends to be directed toward the transducer in this view, allowing a parallel intercept angle between the pulsed Doppler beam and hepatic vein flow. Hepatic vein flow is assumed to be representative of inferior vena caval flow, because both enter the right atrium without intervening venous valves. Direct study of inferior vena caval flow is limited by a nearly perpendicular intercept angle.

Right atrial inflow also can be recorded in the superior vena cava from the suprasternal notch window. From the standard aortic arch view, the transducer is angulated toward the patient's right to visualize the superior vena cava adjacent and slightly anterior to the ascending aorta. The pulsed Doppler sample volume is positioned in the superior vena cava, with adjustment of transducer angle and sample volume depth to obtain a well-defined velocity curve. As for other inflow patterns, wall filters are minimized (as allowed by signal-to-noise ratio) to demonstrate the low velocity

flows associated with atrial filling.

From both the superior vena cava and hepatic vein recordings, it is important to distinguish respiratory variation in the Doppler curves due to respiratory variation in the angle between the ultrasound beam and blood flow direction from true variations in atrial filling volumes. The hepatic vein is small, so several positions often need to be tried to find one that maintains the sample volume in the hepatic vein throughout the respiratory cycle.

The physiologic factors that affect left atrial filling also affect right atrial filling, although (as for ventricular fill) less attention has been focused on physiologic parameters affecting the right side of the heart. Respiratory variation in right atrial filling typically is much more prominent than the respiratory variation seen in left atrial filling.

Alternate Approaches to Evaluation of Diastolic Dysfunction

Despite the numerous potential shortcomings of Doppler echocardiographic evaluation of diastolic filling, it has great promise as a repeatable, non-invasive, widely available method for evaluation of diastolic function. Techniques used in the research laboratory (time constant of relaxation, pressure-volume curves, etc.) rarely are applicable to clinical patient treatment. The other available clinical modalities for evaluation of diastolic function include.

- Direct intracardiac pressure measurements
- Contrast angiographic filling curves based on frame-by-frame volume calculations, and
- Radionuclide high-resolution time-activity curves

Basic Principles of Right Ventricular Tissue Doppler Imaging:

The motion of a muscle, is performed only by the Carnous fibers, and each Carnous fiber has a power of contracting itself... The force of the whole Muscle is but an aggregate of the contractions of each particular fiber.

—William Croone in De ratione motus musculorum (On the Reason of the Movement of the Muscles), 1664.

The tissue Doppler imaging (TDI) method depicts myocardial motion (measured as tissue velocity) at specific locations in the heart. Tissue velocity indicates the rate at which a particular point in the myocardium moves toward or away from the transducer. Integration of velocity over time yields displacement or the absolute distance moved by that point. Tissue Doppler– derived velocity can be obtained via pulsed Doppler (by placing a sample volume at a particular location), M-mode Doppler, or 2-dimensional color Doppler. Color Doppler acquires tissue velocity information from the entire sector, and thus, multiple sites can be interrogated simultaneously. Although all of these methods yield the same mechanical information, differences in the peak values exist. Pulsed Doppler measures peak velocity, which is 20% to 30% higher than the mean velocity measured by color Doppler. This difference should be considered when one estimates left ventricular filling pressure using the E/e' ratio. Frame rates are highest with the M mode, lower with pulsed Doppler, and lowest with color Doppler TDI. Tissue Doppler has been validated extensively and examined in a variety of cardiac pathologies. Although initial work reported tissue velocity from the septal or posterior wall in the parasternal projections, recent work almost exclusively interrogates tissue

velocities in the longitudinal direction (apical projections). In the longitudinal direction, myocardial motion is such that the apex is generally immobile, whereas the base moves toward the apex in systole and away from the apex in diastole. This differential motion between base and apex results in a velocity gradient along the myocardial wall, with the highest velocities at the base and low or zero velocity at the apex.

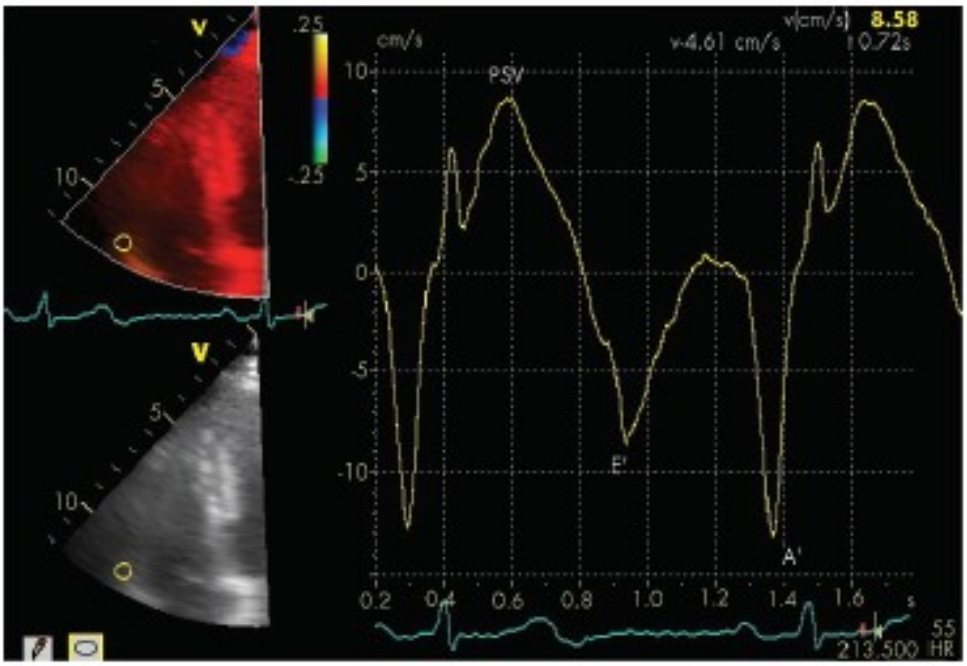

Figure 5 Tracing derived from colour coded tissue Doppler imaging with the sample placed at the level of the tricuspid annulus of the RV free wall, demonstrating peak systolic velocity (PSV), and diastolic velocities (E' and A'). *Ref: Reproduced from Heart 2006;92(supp.I):21)*

In the longitudinal plane, tissue Doppler (TD) assessment of the right ventricular is generally performed by placing a 3–5 mm pulsed Doppler sample volume approximately 1 cm toward the right ventricular apex from the lateral tricuspid valve annulus in the apical four chamber view. Doppler filters are then adjusted to exclude blood velocities, and, in this way, right ventricular wall velocities are preferentially measured and displayed.

Taking into account the normally marked longitudinal excursion of the right ventricular free wall, it is recommended to place the sample volume 1 cm apical to the tricuspid annulus during ventricular systole in order to exclusively measure right ventricular velocities (and not right atrial velocities). Newer modalities that allow "tagging" of a specific area of right ventricular myocardium in order to measure its velocities throughout the cardiac cycle—such as tissue speckle imaging— may obviate such motion-related velocity variations. Several technical issues are of utmost importance in the performance of right ventricular TDI, in order to correctly measure tissue velocities which are as follows (68):

a. correct alignment of the Doppler sample volume to be parallel with the right ventricular lateral wall in order to avoid underestimation of TD velocities (a maximum angle $\theta < 20$ degrees is generally required)
b. minimization of Doppler gains to reduce spectral broadening (for pulsed spectral modality), which can result in the overestimation of TD velocities
c. use of as high a frame rate as possible, (≥100 frames per second)
d. correct timing and identification of TD waves.

As in TDI of the left ventricle, there are five major deflections that are visualized on TD imaging of the right ventricular tricuspid annulus: the isovolumic contraction wave, systolic velocity (S), isovolumic relaxation wave, early diastolic velocity (E'), and late diastolic velocity (A'). When performed using a high frame rate, TD right ventricular imaging is particularly amenable to timing of right ventricular events, resulting in measurements of isovolumic contraction and acceleration, relaxation, and ejection times, lending itself to calculation of the right ventricular myocardial performance (Tei)

Review of the Data on Right Ventricular Tissue Doppler Imaging :

Right Ventricular *Tissue Doppler*

TDI allows quantitative assessment of right ventricular systolic and diastolic function by means of measurement of myocardial velocities. There are many studies which used pulsed wave TDI to examine right ventricular function. Two dimensional colour coded TDI, allows analysis of multiple segments simultaneously. The normal TD right ventricular velocities has already been established. Alam et al.,(69) studied systolic and diastolic velocity profiles of the left ventricle and right ventricular using spectral TD in 62 healthy subjects in three different age groups. Compared to lateral mitral annular S (11.1 ± 2.9 cm/sec), right ventricular S was higher (15.2 ± 1.9 cm/sec). For normal subjects aged >40 to <60 years of age, right ventricular S by pulsed, spectral TD was 15.2 ± 1.9 cm/sec, E' was 15.7 ± 3.4 cm/sec and A' was 15.2 ± 3.4 cm/ sec. The intra- and interobserver variability was 4% and 6%, respectively. Lindqvist et al. (70) analyzed 255 healthy subjects over a wide age range (20–90 years), with similar findings. Kukulski et al. (71), using color TD imaging, found that the mean right ventricular S at the basal free wall was 11.0 ± 2.1 cm/sec, at the mid segment, 8.5 ± 2.0 cm/sec, and at the apical segment, 4.9 ± 1.8 cm/sec. TD reference values for the right ventricle have also been established in the pediatric population. At the basal right ventricular free wall, S was 10.0 ± 3.0 cm/sec, E' was 13.0 ± 3.2 cm/sec, and A' was 8.7 ± 2.5 cm/sec. Therefore, in healthy individuals, normal longitudinal velocities at the basal right ventricular lateral wall are, generally speaking and assuming correct technique, ≥14 ± 2 cm/sec for spectral TD, and ≥10 ± 2 cm/sec for color TD imaging (68).

The method to measure and their appearance is as shown in Fig.6.

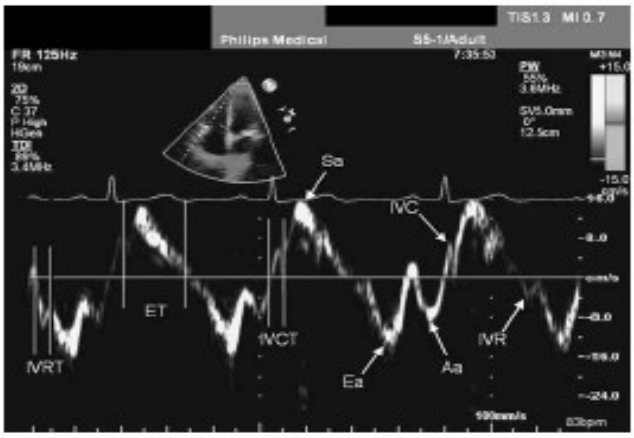

Figure 6. *Tissue Doppler profile of the right ventricle in a healthy young adult. The normal velocities in this subject using*
tissue Doppler pulsed spectral imaging are: Sa(S) = 16 cm/ sec, Ea(E') = 15 cm/sec, and Aa(A') = 10 cm/sec. Aa = late diastolic velocity;
Ea = early diastolic velocity; ET = ejection time; IVC = isovolumic contraction velocity; IVCT = isovolumic contraction time;
IVR = isovolumic contraction velocity; IVRT = isovolumic relaxation time; and Sa = systolic velocity.

Ref: Reproduced from Echocardiography 2007;24(5):524

In patients with inferior myocardial infarction and right ventricular involvement, the tricuspid lateral annular systolic and early diastolic velocities were significantly reduced when compared to healthy individuals and patients without right ventricular involvement. In heart failure patients, the reduction of tricuspid annular systolic velocity is associated with the severity of right ventricular dysfunction. Moreover, non-invasive estimation of right atrial pressure is possible using trans-tricuspid pulsed wave Doppler and TDI (E/E', right atrial pressure = 1.76 (E/E') – 3.7) (72). In hypertrophic cardiomyopathy, subclinical involvement of the right ventricle is also evident by a reduction of tricuspid annular peak systolic and early diastolic velocities and reversal of tricuspid annulus E'/A' ratio.

Besides assessment of right ventricular function, TDI does also permit assessment of ventricular dyssynchrony. This has been extensively demonstrated in the

left ventricle, but the prevalence and haemodynamic consequences of right ventricular dyssynchrony in cardiac disease are not well defined.

Strain rate imaging

While the assessment of longitudinal strain from the apical views is feasible in the clinical setting, the analysis of right ventricular radial deformation from the parasternal window turned out to be difficult. It is hampered by near-field artifacts caused by the close proximity to the transducer and by the thin wall thickness, which requires an extremely small computational distance of less than 5 mm for strain rate measurements. In healthy individuals, Right Ventricular longitudinal velocities demonstrated the typical baso-apical gradient with higher velocities at the base; also, right ventricular velocities are consistently higher as compared to the left ventricle. This can be best explained by:

1. the differences in loading conditions and compliance with a lower afterload in the Right Ventricle
2. the dominance of longitudinal and oblique myocardial fibres in the right ventricular free wall(73).

In contrast to the homogenously distributed deformation properties within the left ventricle, the strain rate and strain values are more inhomogeneously distributed in the right ventricle and show a reverse baso-apical gradient, reaching the highest values in the apical segments and outflow tract.

This pattern can be best explained by the complex geometry of the thin-walled, crescent shaped right ventricle and the more inhomogenous distribution of regional wall stress if compared to the thick-walled, bullet shaped left ventricle. In an elegant animal

experiment, Jamal et al (74) compared echocardiographic strain rate imaging results to sonomicrometry and demonstrated the feasibility of the echo technique to quantify changes in right ventricular contractile function. Doppler derived strain measurements correlated well to sonomicrometry segment length measurements both in the inflow and outflow tract of the Right Ventricle and under different loading conditions. An acute increase in right ventricular afterload led to an increase in right ventricular myocardial strain rate, a measure of contractile function, and to a decrease in peak systolic strain, indicating a decrease in right ventricular stroke volume. Importantly, not only the absolute values changed, but also the strain profile after pulmonary artery constriction demonstrated a shift of myocardial shortening from early-mid to end systole or even early diastole (postsystolic shortening).

Dambrauskaite et al. (75) published a case study on the changes in regional right ventricular myocardial function after bilateral lung transplantation in a patient with primary pulmonary hypertension. Conventional echocardiography showed a significant improvement in right ventricle size and global function after successful transplantation, but strain rate imaging revealed that the functional improvement was limited to the apical, trabecularised portion of the right ventricle and that the smooth inlet segment did not improve after afterload reduction. Before transplantation, peak systolic strain in the apical segment was significantly delayed and occurred in the early diastolic phase after tricuspid valve opening. After transplantation, with after load reduction, it was shifted towards the systolic ejection period and occurred even before pulmonary valve opening, thus confirming the experimental findings by Jamal et al. (74) Furthermore, preliminary data in patients with pulmonary hypertension suggested that in a compensated patient,

peak systolic strain rate correlated with peak systolic pulmonary artery pressure and that regional function will first exhibit depression in the smooth inlet portion of the right ventricle. In this setting, regional analysis of myocardial function may enable the early diagnosis of imminent right ventricular failure before irreversible damage will occur.

In summary, the available experience on strain rate imaging for the assessment of right ventricular function is limited to small single centre studies and case reports. The technique seems feasible for the quantitative assessment of right ventricular function and may improve understanding of the pathophysiology of different diseases. However, the clinical value for patient management remains to be proven.

Three dimensional echocardiography

The clinical use of three dimensional echocardiography has been hindered by the prolonged and tedious nature of data acquisition. The recent introduction of real time three dimensional echocardiography (RT3DE) has revolutionized echocardiography as images may be obtained in just one beat. This has been achieved by the development of a full matrix array transducer (X4, Philips Medical Systems, Andover, Massachusetts, USA), which utilises 3000 elements. This has resulted in

(1) improved image resolution

(2) higher penetration

(3) harmonic capabilities, that may be used for both grey scale and contrast imaging. In addition, this transducer displays ‘‘on-line’’ three dimensional volume rendered images and is also capable of displaying two simultaneous orthogonal two dimensional imaging planes.

The major advantage of RT3DE is that volumetric analysis does not rely on geometric assumptions, as has been the case with two dimensional echocardiography. Quantification of left ventricular volumes and mass using RT3DE has successfully been performed from an apical wide angled acquisition using different methods. A similar approach can be applied for right ventricular evaluation. Data analysis may be performed on-line or offline with dedicated three dimensional software (4D LV analysis, TomTec GMBH, Munich, Germany). Since a data set comprises the entire right ventricular volume, multiple slices may be obtained from the base to the apex of the heart as in the method of discs. This acquisition can then be combined with intravenous contrast agents to improve endocardial border delineation and right ventricular end diastolic and end systolic volumes can be calculated by tracing the endocardial borders similar to MRI

MRI to assess right ventricular function

Magnetic resonance imaging yields high-quality images of the right ventricle and pulmonary arteries, 3D reconstruction of this complex system is achievable, and flow velocities are readily assessed. However, even with this ostensibly ‘perfect’ technique, interpretation of right ventricular parameters should be—age, gender, and BSA—normalized in order to determine normality or severity of abnormality (76).

In recent years, MRI scanners and imaging protocols have developed rapidly. At present, imaging is generally performed on 1.5 Tesla systems, using dedicated cardiac phased-array coils with multiple elements and ECG triggering. Optimal results are obtained using fast breath-hold techniques, echoplanar or balanced fast field echo.

Mogelvang et al. (77) demonstrated the accuracy of MRI to assess right ventricular volumes. The reproducibility of the technique was shown by Grothues et al. (78) who evaluated 60 individuals (20 healthy subjects, 20 heart failure patients, 20 patients with ventricular hypertrophy) on two different occasions. The authors demonstrated an excellent reproducibility for assessment of right ventricular function and right ventricular volumes using MRI. Functional (and anatomical) images of both the left ventricle and right ventricle are commonly obtained in the short axis direction. Alfakih and colleagues (79) compared right ventricular volume measurements in the short axis and in axial directions. The axial orientation resulted in a better intra- and inter-observer reproducibility and may be considered as the preferred direction for assessment of right ventricular function.

MRI can also be used for measurement of flow velocity and volume by phase velocity mapping. Phase velocity mapping is based on gradient-echo pulse sequences in combination with ECG triggering. The phase contrast allows velocity encoding and therefore flow measurements.

Contrast enhanced MRI for imaging of myocardial scar tissue was first described more than 20 years ago. With an inversion recovery turbo field echo pulse, a heavily T1 weighted image is obtained that maximizes the contrast between the scarred (dead) and normal myocardium; accordingly scarred myocardium appears bright whereas normal myocardium is dark. Recent studies have reported excellent correlations between scar tissue on MRI and postmortem analysis of infarcted myocardium. The majority of studies focused on assessment of scar tissue in the left ventricle, but Sato

and colleagues (80) demonstrated the feasibility of MRI for assessment of scar tissue in the right ventricle. An example of contrast enhanced MRI is to assess right ventricular scar formation in a patient with inferior infarction with right ventricular involvement. Estimates of pulmonary pressure can be derived from pulmonary artery distensibility, but the inability to measure pressure directly and limitations in respect of lung parenchymal imaging mean that this will never be a stand-alone imaging technique. Magnetic resonance imaging is already the imaging technique of choice for the evaluation of arrhythmogenic right ventricular dysplasia. This is of special relevance to those caring for patient with pulmonary hypertension, as this condition is associated with impaired contraction of and dilation of the right ventricle in the absence of increased pulmonary pressure. In the setting of pulmonary hypertension, combinable magnetic resonance (CMR) shows increased right ventricular mass and volume indices, as well as reduced LVEF/RVEF, compared with healthy volunteers. Following these preliminary studies, Saba et al. (81) found that a ventricular mass index of 0.6 (RV mass divided by LV mass) had a sensitivity of 84% and specificity of 74% for the detection of pulmonary hypertension, albeit in a relatively small study of 26 patients. Despite these encouraging findings, MR still has no role in establishing the diagnosis of pulmonary hypertension, as exemplified by the findings of Roeleveld et al. (82) . In 44 patients with proven pulmonary hypertension, none of the currently proposed methods for assessing pulmonary pressures perform well compared with direct pressure measurement (pulse wave velocity, cross-sectional area of the pulmonary artery, acceleration time, acceleration time/ejection time,

and ventricular mass index). While diagnosis may be beyond the scope of MRI at

present, there

is much greater potential for this technique, in terms of monitoring the impact of therapy. A recent study in 25 patients with chronic obstructive pulmonary disease suggests that RV mass

increases before baseline pulmonary pressure increases or RVEF decreases. Wilkins et al. (83)

have recently used MR scanning in patients treated with sildenafil in addition to conventional

therapy. They demonstrated a modest reduction in right ventricular mass (-8.8 g; 95% CI, -2 to

-16). Greater changes were observed in BNP (Brain Natriuretic Peptide) and 6MWD (6 minute walk distance), thus MRI in this study was less sensitive to the short-term therapeutic response than other available measures. Long-term studies will be required to see whether the MR changes correlate better with outcome, however, in 13 matched patients treated with bosentan, despite similar haemodynamic and 6MWD response no such reduction in RV mass was demonstrated. The long-term follow-up data available to date do not suggest that sildenafil is associated with a superior prognostic impact compared with bosentan, In contrast to the limited scope for MRI in the clinical management of pulmonary hypertension to date; this technique has already contributed significantly to our understanding of the adaptive changes observed in patients with pulmonary hypertension.

Patients with pulmonary fibrosis in the setting of collagen vascular disease have

been shown to have impaired RV diastolic function, but preserved left ventricular diastolic function using CMR. Kuehne et al (84) have combined CMR and invasive pressure measurement techniques to derive right ventricular pressure volume loops. In a study of six patients without severe symptoms, because of pulmonary hypertension, they were found to have increased right ventricular contractility, but reduced right ventricular and left ventricular stroke volumes. Delayed contrast hyper-enhancement of the right ventricular insertion points to the septum and extending into the septum as septal bowing appears has also been described in patients with increasing severity of pulmonary hypertension. Taken together, these findings suggest that abnormalities of right ventricular function appear early in the setting of pressure overload. Diastolic dysfunction occurs first followed by increased contractility and hypertrophy followed by muscle damage and possibly fibrotic change.

Despite the excellent image quality and reproducibility, MRI has some disadvantages: the data acquisition and analysis is rather time consuming, and some patients groups (for example, pacemaker patients) cannot undergo MRI. Still, MRI can currently be considered the most accurate method for assessment of right ventricular size and function and may be well suited for quantification of right ventricular scar tissue following infarction.

Serum markers:

Many small trials have now been published demonstrating the usefulness of BNP (brain natriuretic peptide) or NTproBNP in monitoring the response to therapy of pulmonary artery hypertension, CTEPH (chronic thromboembolic pulmonary hypertension), acute pulmonary embolic disease and even hypoxic lung disease. The potential of natriuretic peptides in assessing and monitoring the impact of therapies on right ventricular stretch is not surprising as they are released in response to pressure and volume overload of the right ventricle. Most trials, to date, are observational, but they consistently demonstrate that falling levels during treatment or follow-up are associated with improved haemodynamics and survival while the converse is found with increasing levels. The threshold determined for the diagnosis of RV strain varies with the population and from study to study but is generally lower than the levels recommended for the diagnosis of left heart failure if one is aiming for high sensitivity, and higher than the recommended if the aim is specificity. In addition, the level associated with a poor outcome at diagnosis or after initial treatment varies among studies. To date, no large prospective trial had been completed evaluating the role of BNP or NTproBNP specifically addressing either of these questions in a homogenous population. From the trials published to date, there is sufficient data to recommend that all patients with pulmonary artery hypertension should have regular monitoring of BNP or NTproBNP, and that one of the aims of therapy should be to achieve near normal levels where possible. Further, the reduction in natriuretic peptide levels should be included as a secondary end point in future drug trials. What we do not yet know are the

precise prognostic implications of failing to achieve low natriuretic peptide levels, and whether one should augment therapy on the basis of this finding alone. Troponin is released from damaged myocytes, and is now the cardiac enzyme of choice for diagnosing myocardial infarction. Troponin is also released in acute cardiac failure and pulmonary embolism. It is hardly surprising that the release in patients with advanced pulmonary hypertension has been associated with a particularly adverse prognosis, unfortunately, to date; only one study has assessed the importance of this marker. Intriguingly, in this trial, norepinephrine and epinephrine levels fared rather poorly as markers of haemodynamic deterioration or death. Exercise assessment of the right ventricle ideally, one would assess right ventricular function during exercise, as the preservation of contractile reserve cannot be measured at rest. As with left ventricular systolic dysfunction, improvement during exercise confers a better prognosis and effort tolerance. Three-dimensional assessment of right ventricular contractile function is difficult enough at rest; similarly complex measures such as the Tei index are not possible in most patients during exercise. In every day practice, the only available measure during exercise is the tricuspid gradient and the change in pressure during exercise has not yet been correlated with clinical outcome. Cardiopulmonary exercise testing provides many measures, the VO2max in particular correlates well with prognosis and quality of life. In expert hands, this is a reproducible technique but differences between centres, mean that in studies such as the STRIDE 1 interobserver variability gave inconsistent results (85). Until there is improved standardization, this technique gives information unique to the unit performing the test. The 6MWD correlates roughly (r ¼ 0.6) with the VO2max even in the best hands only when age and

body mass is taken into account. Thus, it is probably not a measure of the anaerobic threshold but rather a measure of the best sustainable aerobic performance. In advanced pulmonary hypertension, right ventricular contractile reserve is the dominant determinant of maximal cardiac output during exercise. Thus, for any individual, all other factors being equal (arthritis, leg ulceration, and training effects), the direction and magnitude of change of 6MWD should correlate with changes in right ventricular contractile reserve. In this context, it is difficult to understand why changes in 6MWD in response to therapy do not correlate with survival. One possible explanation is that contractile reserve underpins the effort tolerance and other factors in determining myocyte survival. Finally, the response of BNP levels to exercise in patients with right ventricular dysfunction has not been published. However, BNP release with exercise behaves inconsistently in patients with left heart failure so it is not clear whether this is a avenue worth pursuing.

Review of previous studies on mitral stenosis and right ventricular function:

There are not many studies which have used tissue Doppler imaging for assessing RV functions in patients with mitral steosis. Kurtulus et al.(86) studied a group containing 46 mitral stenosis patients and 40 controls. They used pulsed wave DTI (Doppler tissue imaging) to study myocardial velocities at 4 sites of left ventricle and right ventricular free wall annulus. Basic parameters were comparable in both groups. Left atrial size was larger and ascending aorta was smaller in patients with mitral stenosis as compared to controls. The myocardial velocities obtained from left

ventricular wall annulus and then mean values were significantly lower in patients with mitral stenosis.The mean E'/A' ratio obtained from tricuspid annulus was less than 1 and lower than control group, but it did not achieve stastical significance. This was among the first few studies to demonstrate that pure mitral stenosis results in significant reduction of left ventricular systolic and diastolic myocardial velocities. There has been one more study from Mehta et al.(87) which used DTI and compared 30 normal controls from 25 patients with pure mitral stenosis for change in right ventricular myocardial velocities pre and post percutaneous mitral commissurotomy. They found that there were marked abnormalities in deformation characteristics of RV free wall which persisted in the immediate period following commissurotomy which could explain the persistence of right sided congestion noted in some patients. Saricam et.al. (88) did a similar study as ours where they correlated RV myocardial velocities and functional class in patients with mitral stenosis with pulsed wave tissue Doppler. They classified patients into 2 groups as according to symptoms. The symptomatic group had E'/A' ratio of less than 1(0.76+/-0.17) which was statistically significant from the other group suggesting right ventricular diastolic dysfunction. They also showed differences in right ventricular E', A' and IVRT values, concluding a significant contribution of right ventricular diastolic function in symptom class. Bove et al. (89) presented a study based on 14 patients who underwent right and left heart catheterization including biplane right and left ventriculography. It revealed that right ventricular systolic pressure was elevated in mitral stenosis group, but right ventricular end diastolic volume index and ejection fraction were comparable. Patients with mitral stenosis had slightly higher right ventricular end diastolic pressure (5.8+/-1.7 v/s 2.4+/-0.77) but it was not statistically

significant. A plot of right ventricular stroke volume versus end diastolic volume, which removes pressure from the performance index, revealed similar performance between the two groups. These early studies showed that right ventricle maintains normal volume and contractile performance in the presence of pressure overload induced by mitral stenosis and gradually progress to right ventricular failure. Literature shows that the left ventricle which faces chronic pressure overload passes through the phases of compensatory hypertrophy, diastolic dysfunction and decompensation very similar to right ventricle. At the end the authors concluded that although normal right ventricular pump function was demonstrated they were unable to state that muscle function was also normal. They thought a disparity between pump and muscle performance may occur and normal performance may be maintained by hypertrophy of poorly performing muscle units, this probably was an indication of diastolic dysfunction as we know today. Donald et.al. (90) assessed 20 patients with isolated mitral stenosis in sinus rhythm by supine, symptom limited equilibrium radionuclide ventriculographic studies. All the patients had normal left ventricular ejection fraction at rest (>/=50%) which rose significantly during exercise (64+/-9% v/s 74+/-11%, $p<0.001$). This rise in left ventricular ejection fraction was mediated solely by decrease in exercise left ventricular end-systolic volume ($p<0.01$). There was a significant decrease in exercise end-diastolic volume ($p<0.01$) which limited the increase in ejection fraction, but cardiac output rose according to heart rate alone. The right ventricular ejection volume did not rise with exercise due to an increase in end systolic volume. It was noted that neither resting nor exercise associated left ventricular ejection fraction was affected by the severity of mitral stenosis. Also the right ventricular end-systolic volume, instead of decreasing

normally rose with exercise, while end-diastolic volume increased slightly. Thus the authors concluded that the attenuated response of right ventricular ejection fraction was likely due to a change in loading conditions associated with exercise. Cohen et al.(91) also studied right ventricular function in a similar group of patients and also found that loading conditions determine the right ventricular response to exercise; however there is a possibility that irreversible right ventricular myocardial damage from hemodynamic stress contributes to abnormal systolic function in certain individuals. Gorlin et.al. (92) did a very early study in eight patients with mitral stenosis by cardiac catheterization and looked at mitral valve area, right atrial and left ventricular work, right atrial pressure, pulmonary capillary pressure and cardiac index at rest and during exercise. The study showed that pulmonary arteriolar resistance showed no consistent change on exercise, the average values at rest and during exercise being identical. Right ventricular work was elevated at rest and it increased on exercise. All patients had elevated right atrial mean pressure at rest and rose in two of four patients in whom it was studied. This again points to the diastolic function or loading status of right ventricular which decides its output. Anthony et.al.(93) presented their study which had 45 patients (26 with mitral stenosis and rest normal volunteers.) who were assessed with exercise gated radionuclide angiography with special stress on right ventricular function. They found that, in both controls and mitral stenosis group the left ventricular and right ventricular ejection fraction rose during exercise but the percentage change was more in normal and the value was significant($p<0.05$). The lack of an appropriate rise in ejection fraction, however was achieved differently by each ventricle. The left ventricle showed a fall in end diastolic count whereas the right ventricular showed a rise in end systolic

count. They suggested that, the left ventricular contractility was normal and lack of rise in ejection fraction was caused by an alteration of loading, that is, end-diastolic volume or preload, resulting from the inability of the left ventricle to fill adequately because of the mitral stenosis. The rise in right ventricular end systolic count more likely reflected a fall in contractile state in presence of increased afterload.

MATERIALS AND METHODS

Study Design :

This was a prospective descriptive trial performed over 8 months period from February 2007 to October 2007.

Setting :

CMC Vellore is a 2000 bedded tertiary care teaching hospital. Patients were recruited from the outpatient department. 51 consecutive patients with moderate to severe MS and sinus rhythm were enrolled for the study.

Subjects :

Inclusion Criteria

1. Moderate to severe mitral stenosis with sinus rhythm on ECG.

Exclusion Criteria

1. Presence of coronary artery disease (angina, and/or ECG sign of ischemia) and two dimensional wall motion abnormalities.
2. Diabetes mellitus
3. Sinus tachycardia
4. Atrial fibrillation
5. More than mild aortic or mitral and moderate tricuspid regurgitation
6. Pulmonary arterial hypertension (TR gradient > 40mmHg)
7. Lung disease - according to history, physical examination and pulmonary

function tests

8. NYHA IV functional class
9. Inadequate echocardiograms

Clinical Assessment:

All patients were interviewed individually for history, duration and severity of symptoms. They were assessed by New York Heart Association (NYHA) functional classification (94) and divided into two groups. They were thereafter subjected to thorough clinical examination for valvular lesions and pulmonary findings and were then subjected for standard echocardiographic study, Eligible patients for inclusion were informed about the study and informed consent was obtained.

Echocardiographic Protocol:

Group I (asymptomatic group) consisted of 20 patients with NYHA class I and group 2 (symptomatic group) had 31 patients with class II- III symptoms. Standard Doppler echocardiography and tissue Doppler were performed with the subjects in left lateral decubitus position, by a 5MHz probe on iE -33 (Philips Medical Systems, Andover, Massachusetts, USA). The variable frequency phased array transducer was used for two-dimensional, M-mode and Doppler imaging. All values used were the average obtained from three cardiac cycles, to minimize the difference during the breath cycle. M-mode and two-dimensional quantitation of the left ventricle was performed according to the standards of the American Society of Echocardiography (95, 96). Mitral valve area (MVA) was determined by the pressure-half-time method (97). The

study included patients with MVA < 1.5cm². Transmitral velocities and pressure gradients were recorded by the continuous wave Doppler. Doppler colour flow imaging was used for detection and semi quantisation of the tricuspid, mitral and aortic regurgitation. right ventricular global systolic function was assessed by tracing the right ventricular endocardial border at end diastole and end systole to calculate the ejection fraction. All patients who participated in the study had right ventricular EF >= 40%. TDI was performed in apical four-chamber view, by placing the sample volume 1cm ablve lateral tricuspid annulus. Tissue Doppler pattern was characterized by a positive myocardial systolic wave(S) and two negative diastolic waves - early (E') and atrial (A'). Tissue Doppler systolic indexes included myocardial peak velocity of S (m/sec) and isovolumic contraction time (IVCT) (IVCT was measured from the onset of ECG QRS to the beginning of S). Diastolic indexes included myocardial early (E') and atrial peak velocities (A') (m/sec), E'/A' ratio and isovolumic relaxation time (IVRT) (msec) (IVRT was defined as the time interval occurring between the end of S and the onset of E'. The filter settings were kept low (50Hz), and gains were adjusted at the minimal optimal level to minimize noise and eliminate the signals produced by the transmitral flow.

A Doppler velocity range -15 to +15cm/sec and high frame count (>100 frames per second) was selected for this study. Special care was taken for correct alignment of the Doppler sample volume. In the TDI images the s wave duration was measured as ejection time (ET), whereas IVCT and IVRT were measured as mentioned before. The Myocardial Performance Index (MPI) was calculated with the same formula.

MPI = (IVRT + IVCT)/ET

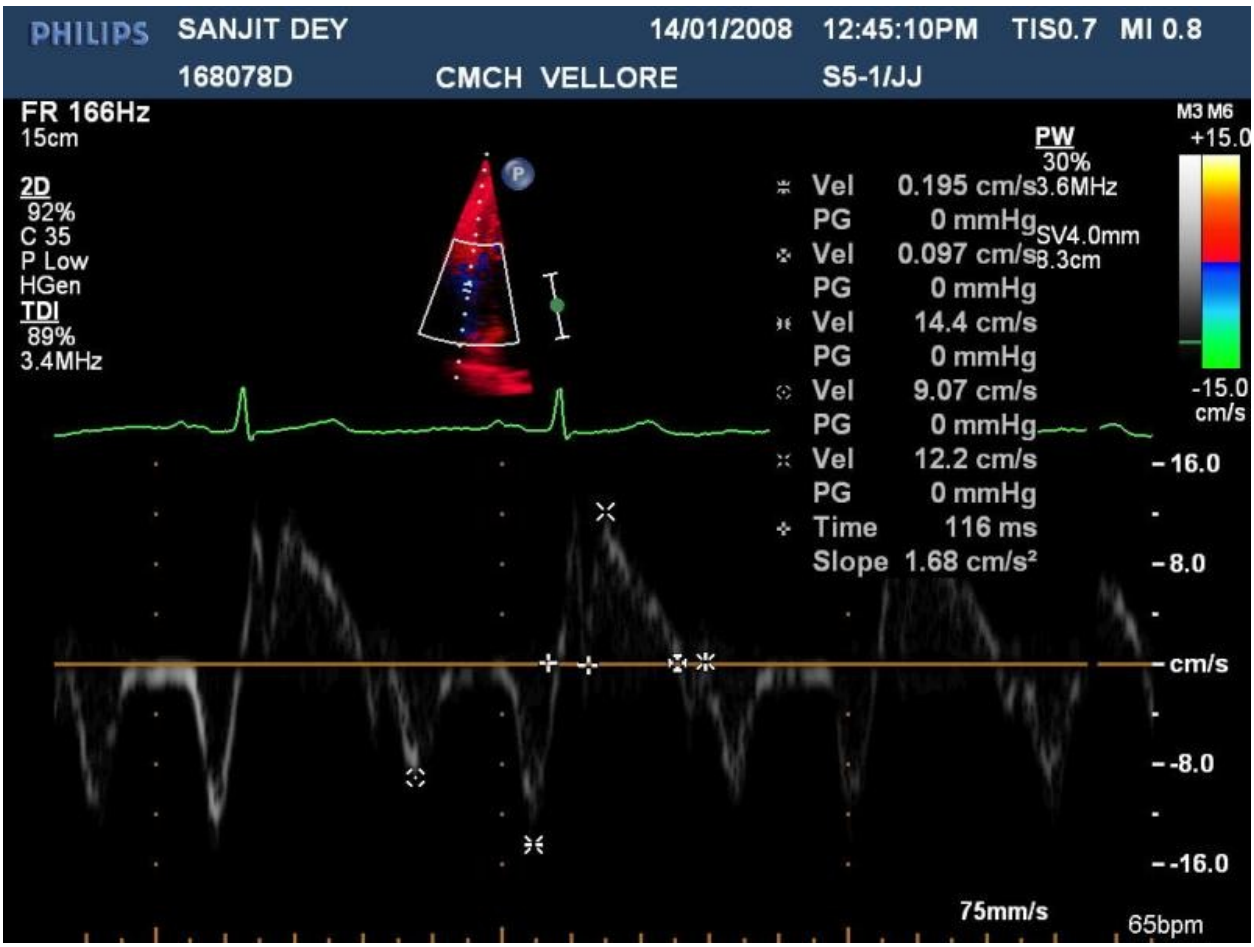

Figure 4 : Different parameters as measured during study.

Statistical Analysis :

All statistical analyses were performed by SPSS for windows release 11.0 (Chicago,Illinois,USA). Categorical variables are presented using frequency and percentage,continuous variables are described using mean and standard deviation. Comparisions between groups were performed using standard student's't' test. Variables that were continuous but not normally distributed were analysed using Mann-

Whitney test. Assosiation between categorical variables were assessed using chi-square test with Yates correction. Relationships of continuous variables with others are displayed using the confidence interval plots. Multiple linear regression was performed to evaluate the simultaneous and independent contribution of the covariates towards E'/ A' ratio and the partial regression coefficients are presented with their respective levels of significance. A p-value of less than 0.05 was considered statistically significant.

RESULTS

During the period February 2007 to October 2007, 51 patients with mitral stenosis and sinus rhythm were included in the study. They were divided into two groups. Group I (patient with NYHA class I symptoms) and Group II (patients with NYHA class II – III symptoms). Group I had 21 patient and Group II had 30 patients. Patients in group II, were significantly older when compared to Group I and it was statistically significant (31.81+/-2.28 years v/s 39.63+/-1.89 years,$p<0.05$).

The two group were comparable in sex (male / female in Group I was 6/15 and 13/17 in Group II $p \geq 0.05$), prior balloon mitral valvotomy (BMV) or closed mitral valvotomy (CMV) (5 in Group I and 7 in Group II, $p \geq 0.05$) mitral valve score, mean mitral valve area, tricuspid regurgitation gradient, mitral regurgitation dimension, left ventricular ejection fraction and transmitral mean gradient. The left atrial dimension was higher in group II as noted in table 1.

RV parameters as measured by colour TDI are presented in table 2. Statistical difference was not determined in systolic parameters (S, IVCT) between the two groups. However, values of IVRT (Group I – 68.57 + /- 16.39 Vs Group II – 81.20 + /- 26.76, $p < 0.05$), A' wave amplitude (Group I – 13.25 + /- 3.48 Vs Group II – 15.17 + /- 2.81, $p < 0.05$) were higher. Whereas E' wave amplitude was lower (Group I – 14.76+/-4.62 Vs Group II- 10.55+/-3.37, $p<0.05$) in Group II. Right ventricular E'/A' ratio (Group I – 1.17 +/- 0.43 Vs Group II – 0.70+/- 0.19, $p < 0.001$) was lower in symptomatic group and was highly significant. Figure 5,6, and 7 are confidence interval plots pictorially showing the minimal overlap between parameters suggestive of strong association of E', A' and E'/A' between the groups.

Table 3 shows association of right ventricular function parameters with mitral valve area (MVA) less than 1 as cut-off , and we find that neither the systolic nor diastolic right ventricular functions have any statistically significant difference between both groups in this study . As far as left atrial size is concerned it does have significant correlation with E' and E'/A' ratio with a cut-off of 4 cm between both groups (Table-4). Also we notice that people who underwent either BMV/CMV in past had a lower E' velocity as compared to those who never had any mitral intervention (Table-5). In our study we were not able to show any correlation between RV Tei index and systolic or diastolic parameters of RV taking 0.5 as cut-off (Table-6). Even the index did not show any significant association with symptom class. When we classified the subjects into two groups with E'/A' ratio of less than 1 as cut-off we found that patients who had diastolic dysfunction also had lower "s" wave velocity and a higher IVCT and RV ejection time though it did not achieve statistical significance. This indicates that subjects with diastolic dysfunction probably has systolic impairment too when compared to other group but it needs larger study to confirm statistically. IVRT was higher in group with E'/A' ratio of less than 1 with $p<0.05$. Even though Tei index was higher and MVA was smaller in group with E'/A'<1, it did not achieve significance; however age and symptom class was higher in this group, with $p<0.05$ (Table-7) . Mitral valve gradient of 10 mm Hg was taken to classify all subjects and we still could not achieve any statistical significance in right ventricular systolic and diastolic parameters, except with left atrial size which was larger in patients with higher gradient (Table-8). We tried to assess independent correlation of E'/A' ratio of less than 1 and found that MVA, TR gradient, Tei index and MV gradient had no association while age and LA size did have

independent association.

Table 1: Baseline characteristics:

Variable	Group I (NYHA class I)	Group II (NYHA class II – III)	p value
Age	31.81 ± 10.45	39.63 ± 10.39	$p \leq 0.05$
Gender (M/F)	6/15	13/17	$p > 0.05$
Mitral valve area	01.11 ± 00.28	01.02 ± 00.24	$p > 0.05$
MV mean gradient	12.85 ± 06.90	13.50 ± 05.12	$p > 0.05$
Left atrial size	40.67 ± 06.23	46.73 ± 06.85	$p < 0.05$
TR gradient	23.76 ± 10.63	25.87 ± 09.82	$p > 0.05$
RV end diastolic volume	24.86 ± 10.94	27.27 ± 12.41	$p > 0.05$
RV end systolic volume	11.71 ± 05.13	12.90 ± 07.35	$p > 0.05$
RV ejection fraction	57.14 ± 12.35	56.10 ± 11.02	$p > 0.05$

Table 2 : RV Tissue Doppler parameters between both groups

Variable	Group I (NYHA class I)	Group II (NYHA class II – III)	p value
S wave velocity	12.24 ± 02.70	10.91 ± 02.65	$p > 0.05$
Tissue Doppler E'	14.76 ± 04.62	10.55 ± 03.37	$p < 0.01$
Tissue Doppler A'	13.25 ± 03.48	15.17 ± 02.81	$p < 0.05$
Tissue E'/A'	01.17 ± 00.43	00.70 ± 00.19	$p < 0.01$
RV IVCT (Isovolumic contraction time)	88.62 ± 24.98	91.30 ± 25.18	$p > 0.05$
RV Ejection Time (ET)	257.57 ± 29.84	282.10 ± 37.73	$p < 0.05$
RV IVRT	68.57 ± 16.39	81.20 ± 26.76	$p < 0.05$
RV Tei Index	00.60 ± 00.12	00.62 ± 00.17	$p > 0.05$

Table 3 : Correlation between RV parameters and MVA (cut off 1cm²)

Variable	MVA > 1cm²	MVA < 1cm²	p value
S wave velocity	11.42 ± 02.97	11.50 ± 2.54	p > 0.05
Tissue Doppler E'	12.56 ± 04.98	12.04 ± 3.93	p > 0.05
Tissue Doppler A'	14.26 ± 03.20	14.48 ± 3.28	p > 0.05
Tissue Doppler E'/A'	00.91 ± 00.39	0.88 ± 0.39	p > 0.05
RVIVCT	93.04 ± 25.04	87.67 ± 24.93	p > 0.05
RVIVRT	75.33 ± 27.72	76.59 ± 20.01	p > 0.05
RV ET	269.46 ± 38.03	274.26 ± 35.60	p > 0.05
RV Tei Index	00.62 ± 00.16	0.60 ± 0.14	p > 0.05

Fig:5 Confidence plot showing correlation of E' between both groups.

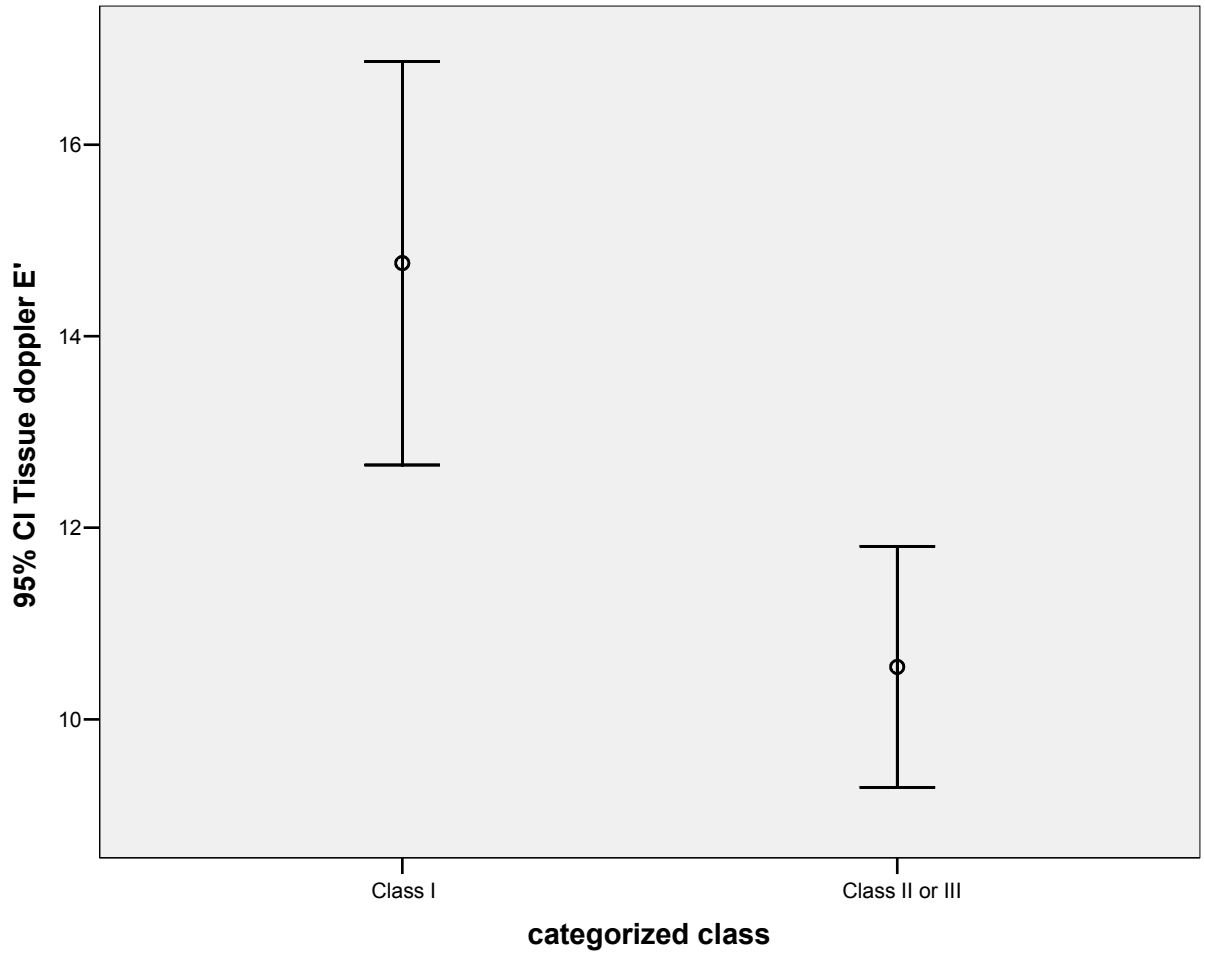

Fig:6 Confidence plot showing relation of A' between both groups

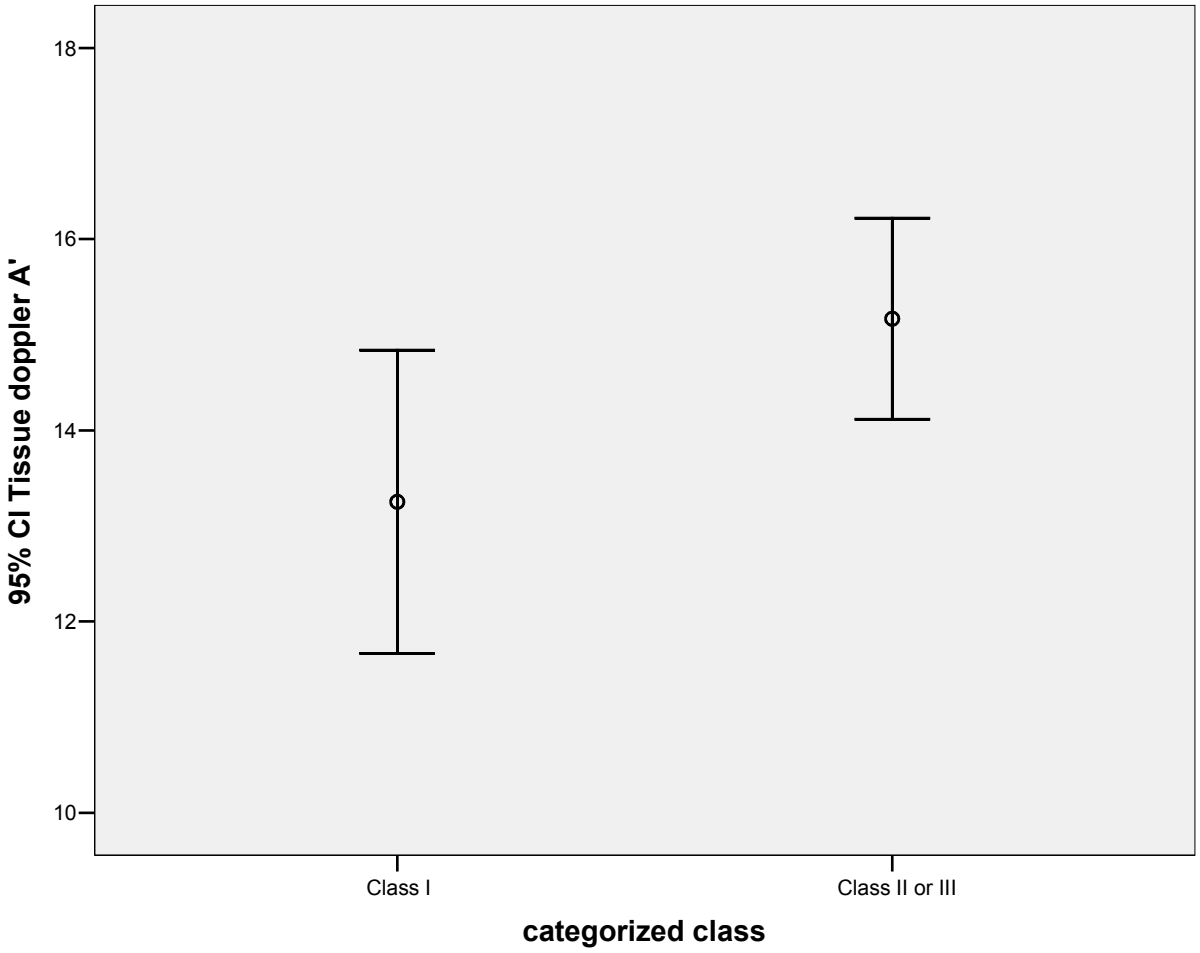
95% CI Tissue doppler A'
18
16
14
12
10
Class I
Class II or III
categorized class

Fig :7 Confidence plot of E'/A' ratio between both groups :

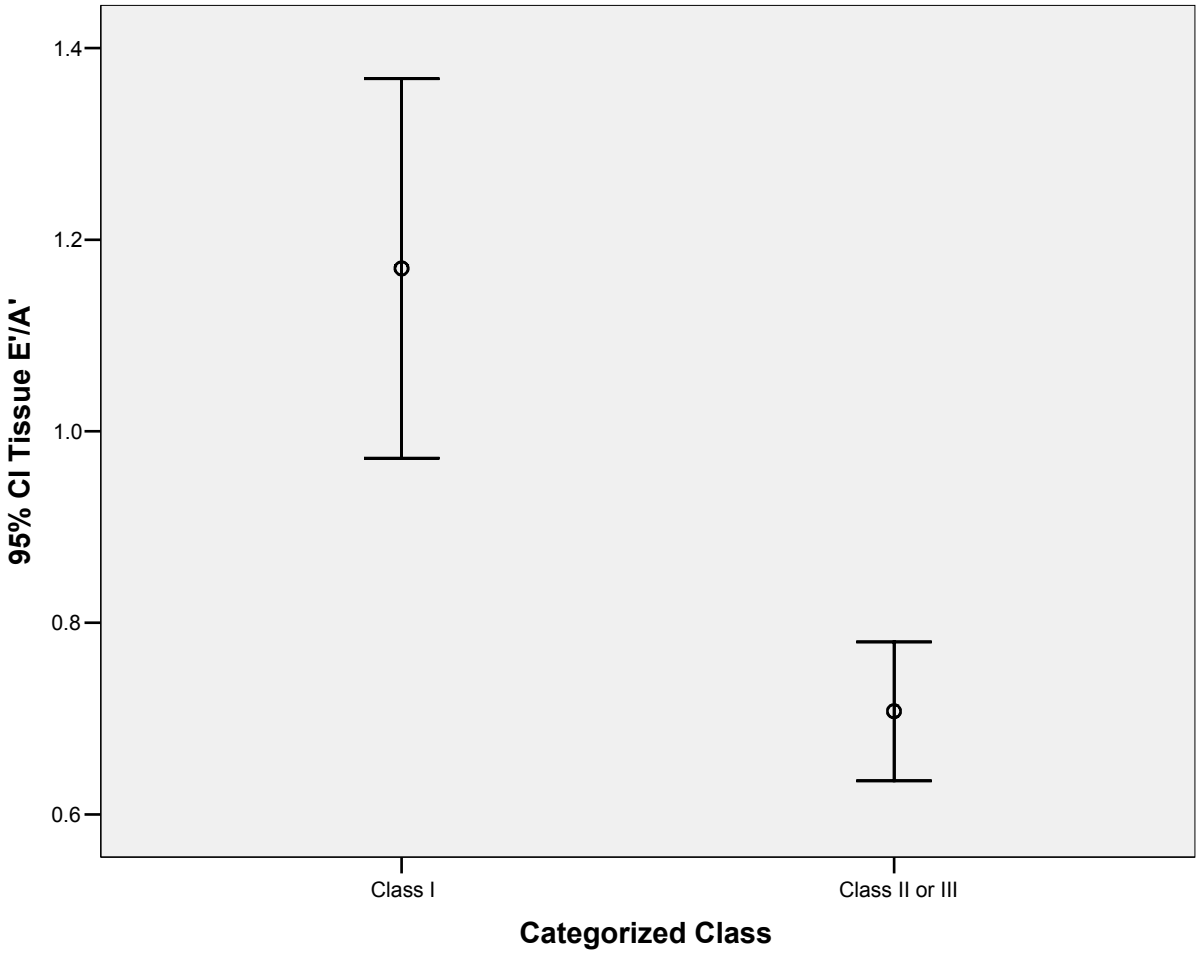

Table 4 : **Correlation between RV parameters and Left atrial (LA) size (cut off 40mm)**

Variable	LA>/=40	LA<40	p value
S wave velocity	11.38 ± 2.83	11.61± 2.59	p > 0.05
Tissue Doppler E'	11.30 + 4.15	14.09 + 4.43	p < 0.05
Tissue Doppler A'	14.73 + 2.99	13.74 + 3.59	p > 0.05
Tissue Doppler E'/A'	0.79 + 0.34	1.08 + 0.40	p < 0.05
RVIVCT	89.21 + 24.47	92 + 26.23	p > 0.05
RVIVRT	78.30 + 22.10	71.78 + 26.55	p > 0.05
RV ET	278.88 + 35.11	259.39 + 36.49	p > 0.05
RV Tei Index	0.60 + 0.14	0.63 + 0.17	p > 0.05

Table 5: **Correlation between previous BMV / CMV and RV parameters**

Variable	BMV / CMV	No intervension	p value
S wave velocity	10.75 ± 2.05	11.68 ± 2.89	p > 0.05
Tissue Doppler E'	10.03 ± 2.66	12.97 ± 4.64	p < 0.05
Tissue Doppler A'	13.08 ± 3.45	14.78 ± 3.08	p > 0.05
Tissue E'/A'	0.86 ± 0.46	0.90 ± 0.36	p > 0.05
RV IVCT	95.83 ± 19.87	88.46 ± 26.21	p > 0.05
RV ET	280.58 ± 40.78	269.36 ± 35.19	p > 0.05
RV IVRT	84.75 ± 28.59	73.31 ± 21.72	p > 0.05
RV Tei Index	0.63 ± 0.15	0.60 ± 0.15	p > 0.05

Table 6: **Correlation between varibles and RV Tei index (cut off 0.5)**

Variable	Tei Index ≥ 0.5	Tei Index < 0.5	p value
S wave Velocity	11.59 + 2.72	11.08 + 2.81	p > 0.05
Tissue Doppler E'	12.33 + 4.44	12.14 + 4.52	p > 0.05
Tissue Doppler A'	14.59 + 3.51	13.77 + 2.12	p > 0.05
LA Size	44.63 + 7.84	43.08 + 4.95	p > 0.05
MVA	1.06 + 0.27	1.04 + 0.22	p > 0.05
MV gradient	12.34 + 4.5	15.84 + 8.41	p > 0.05
Symptom class (Class I / II & III)	17/21	4/9	p > 0.05

Table 7: **Correlation between different variables and E'/A' (cut off ≥ 1)**

Variable	E'/A' ≥ 1	E'/A' < 1	p value
S wave velocity	12.88 + 3.35	10.75 + 2.06	p < 0.05
RV IVCT	86.47 + 27.25	92.06 + 23.82	p > 0.05
IVRT	66.88 + 16.67	80.56 + 25.55	p < 0.05
RV ET	256.24 + 29.80	279.88 + 37.32	p < 0.05
RV Tei Index	0.59 + 0.13	0.62 + 0.16	p > 0.05
MVA	1.12 + 0.27	1.03 + 0.24	p > 0.05
Symptom class (Class I / II & III)	15 / 2	6/28	p < 0.05
Age	29.41 + 9.22	39.91 + 10.24	p < 0.05
LA size	39.59 + 6.15	46.56 + 6.60	p < 0.05

Table 8: **Correlation between RV parameters and mean mitral gradient (cut off 10mmHg)**

Variable	MV gdt ≥ 10	MV gdt < 10	p value
S wave velocity	11.42 ± 3.01	11.57 ± 1.70	p > 0.05
Tissue Doppler E'	12.31 ± 4.87	12.20 ± 2.86	p > 0.05
Tissue Doppler A'	14.40 ± 3.20	14.31 ± 3.37	p < 0.05
Tissue E'/A'	0.88 ± 0.36	0.94 ± 0.44	p < 0.05
RV IVCT	89.13 ± 25.99	93.31 ± 21.96	p > 0.05
RV IVRT	75.92 ± 23.90	76.23 ± 24.12	p > 0.05
RV Tei Index	0.61 ± 0.16	0.60 ± 0.11	p > 0.05
LA size	45.55 ± 7.78	40.38 ± 2.84	p < 0.05

Table 9: **Multivariate linear regression analysis to show any independent correlation between E'/A' and MVA, Tei Index and TR gradient.**

Variable	Partial regression coefficient	p value
MVA	0.237	0.098
TR gradient	0.006	0.30
RV Tei Index	-0.252	0.47
Age	-0.010	0.045
LA size	-0.018	0.015
MV gradient	0.015	0.076

DISCUSSION

The present study shows the importance of colour TDI in analyzing patients who have rheumatic mitral stenosis and right ventricular diastolic dysfunction associated with symptoms. To the best of our knowledge, this is the first Indian report to show association between right ventricular diastolic dysfunction and symptoms in patients with mitral stenosis.

In our study protocol we evaluated 7 useful indices of right ventricular function in patients with mitral stenosis and sinus rhythm by colour TDI.

a. IVCT
b. S wave
c. E'
d. A'
e. E'/A'
f. IVRT
g. Tei Index

It has been proved that RV systolic function is a major determinant of symptoms while effect of right ventricular diastolic function on symptoms is not clear. Rowe et al (98) have shown a survival of 84% in asymptomatic patients and 42% in symptomatic patients with mitral stensois (4). In clinical practice, we quite often come across patients with normal right ventricle systolic function and moderate to severe mitral stenosis who have symptoms while some patients with similar valve area are asymptomatic. Thus the role of right ventricular diastolic function was probed in this study using colour TDI to determine if it can contribute to symptoms.

It is a relatively new technique which is not in-adversely influenced by preload and shows tissue contraction and relaxation rates with high resolution. Tricuspid E' velocity represents relaxation activity of right ventricle, while A' reflects atrial activity. E'/ A' ratio is indication of passive lengthening of myocardial fibres and IVRT suggestive of energy dependent phase of isometric relaxation. When E'/A' is less than 1 it indicates an impairment in ventricular compliance (99). The impairment of diastolic function may be due to increase in pulmonary arterial pressure or ventricular interdependence (110). Rheumatic heart disease by itself can cause right ventricle myocardial involvement and stiffening of fibres. Circala et al. (101) showed by tissue Doppler that right ventricle diastolic functions are affected even in patients who had hypertension as it caused right ventricle hypertrophy while the systolic functions remained normal. In our study too patients had mild hypertension which was similar in both groups. We known that "s" wave and IVCT represents RV systolic function which was comparable in both groups and p value was more than 0.05. This correlated with a similar study done by Saricam et al (88) who used pulse tissue doppler as their investigational mode. They also showed lower values of E', E'/A', IVRT and a high A' value in symptomatic group with significant p value. In contrast to our study their groups were not different in age and the left atrial size was comparable between both groups. In our study, the basic difference is noted in diastolic parameters. In group II the E' velocity was reduced which suggests right ventricle relaxation impairment. We also note that A' velocity is much more in the symptomatic group which indicates increased atrial contribution to diastolic ventricular filling. The E'/A' value which is less than 1 in symptomatic group and highly significant when compared between both groups, suggests impairment of

right ventricle diastolic compliance. It can be noted that IVRT is more prolonged in the symptomatic group and right ventricle diastolic dysfunction is not independently related to mitral valve size, MV gradient,TR gradient or Tei Index but did correlate with left atrial size and age.

This study failed to show statistically significant relation between Tei Index and symptomatic status. The index also did not have significant relation to TR gradient in this study.

Summarizing, this study showed that right ventricular diastolic function as measured by color TDI were impaired in the presence of normal right ventricle systolic function in symptomatic cases with isolated mitral stenosis, whereas diastolic parameters in patient's with class I symptoms and similar mitral valve area and TR gradient remained intact. Thus diastolic dysfunction may be considered to contribute to symptomatic progression of disease. We know that symptomatic patients have poor prognosis and thus right ventricle diastolic function assessment in mitral stenosis may give an idea about prognosis. It can also help us to plan intervention in borderline cases where symptomatic status and mitral valve area do not correlate.

LIMITATIONS

1. We have used Doppler technique where beam alignment with direction of RV free wall is crucial. To achieve this, we have adjusted scanning angle to keep the angle below 20º and have taken an average of three values for every parameter.

2. Although tissue Doppler data can be measured with poor right ventricular visualization it greatly limits derivation of correct myocardial velocities. We have tried and kept right ventricular wall well in view before applying tissue Doppler. Also by taking average of three values we have tried to minimize significant deviation in values.

3. Spectral signal broadening can result in significant overestimation of right ventricular tissue Doppler velocities, potentially leading to overestimation of right ventricular function. We have kept Doppler gains to as minimum as possible to avoid this artifact.

4. The method of estimating right ventricular ejection fraction has been a limitation in this study as we have substituted MRI by echocardiogram, MRI is considered gold standard for right ventricular function. We have assessed right ventricle systolic function by colour TDI also. It has been shown that s wave velocity of $\geq$10+/-3cm/sec correlate with normal RV systolic function (68) and in this study all our patients had higher value than this. Thus we think this limitation is not very important.

5. Sample size: The number of patients is only 51. A larger study needs to be done to confirm findings.

CONCLUSIONS

1. 93% (28 out of 30) of symptomatic and 29% (6 out of 21) of asymptomatic patients had right ventricular diastolic dysfunction in presence of moderate to severe rheumatic mitral stenosis.
2. Right ventricular Tei index did not show any correlation with symptom class in moderate to severe rheumatic mitral stenosis patients.

BIBLIOGRAPHY

1. Carpetis J.R.,Mc Donald M,Wilson NJ, Acute rheumatic fever Lancet, 2005:366:155-68.
2. Carpetis J.R.,Steer A.C.,Mulhouand EK,et al. The global burden of group A streptococcal disease. Lancet Infect Dis 2005;5:685-94.
3. Eloi Marijon, Phalla O, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med 2007;357:470-6.
4. Rowe J.C., Bland E.F., Sprague HB, et al. The course of mitral stenosis without surgery : ten and twenty year perspectives. Ann Intern Med 1960;52:741-9.
5. Feldman T. :Rheumatic Heart Disease. Curr Opn Cardiol 1996;11:126-30.
6. Rigolin V.H. ,Higgenbotham M.B. , Robiolio PA, et.al. Effect of inadequate cardiac output reserve on exercise tolerance in patients with moderate mitral stenosis. Am J Cardiol 1997;80:236-40.
7. Vacek B. J., Stone P. V.,Wolfe M, et al. The value of standardized exercise testing in the non invasive evaluation of mitral stenosis. Am J Med Sci 1986;292(6) :335-43.
8. Bonow R. O.,Carabello B., Deleon AC, et al. ACC/AHA guidelines for the management of patients with valvular heart disease. J Am Coll Cardiol 1998;32:1486-1588.
9. Vincens J. J. ,Temizer D. , Post JR, et. al. Long term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. Circulation 1995;92(9 Suppl.):II 137-II 42.
10. Rigolin V.H. ,Robiolio P.A., Wilson JS, et. al. The forgotten chamber.The importance of the right ventricle. Cathet Cardiovasc Diagn 1995;35;18-28.

11. Nagel E.,Stuber M., Hess O.M., et al. Importance of the right ventricle in vavular heart disease. Eur Heart J 1996;17:829-36.
12. Bossen D. ,Jones K. F., Fisehetti VA, et al. Evidence for two distinct cones of stretococcal M protein and their relationship to rheumatic fever. J Exp Med 1989;169;269-83.
13. Smoot J. C., Barbian K. D., Smoot LM, et. al. Genome sequence and comparative microarray analysis of serotype M18 group A streptococcus strains associated with acute rheumatic fever outbreaks. Proc Natl Acad Sci USA ,2002;99;4668-73.
14. Stollerman G.H. Rheumatogenic streptococci and autoimmunity. Clin Immunol Immunolpathol. 1991;61:131-42.
15. Massel B.F. ,Chute C. G., Walker AM, et al. Penicillin and the marked decrease in morbidity and mortality from rheumatic fever in the United States. N Eng J Med 1988;318:280-6.
16. Krasuski R. A. ,Bush A., Kay JE, et al. C-reactive protein elevation independently influences the procedural success of percutaneous balloon mitral valve commissurotomy. Am Heart J 2003;146:1099-2104.
17. Carabello B.A , Modern Management of mitral stenosis. Circulation, 2005 ;112 : 432 – 7
18. Sainani G.S., Sainani A.R., Rheumatic fever-how relevant in India today? JAPI 2006; 54(Suppl.):42-7.
19. Veasy L.G.,Wiedmeir S.E., Orsmond GS, et al. Resurgence of acute rheumatic fever in the intermountain area of the United States. N Eng J Med 1987;316(8);421-7.
20. Carpetis J.R. The current evidence of the burden of group A Streptococcal disease.

WHO/FCH/CAH/05-07. Geneva: World Health Organization 2004; 1 – 57.

21. Sharma M.,Saxena A., Kothari S S, et al. Acute rheumatic fever in children : experience from a cardiac centre(Abstr.) Indian Heart J 1999;51:652.
22. Mishra T.K.,Rath P.K., Mohanty N K, et. al. Juvenile chronic RHD, our decade long experience(Abstr.). Indian Heart J 1999;51:653.
23. Lalchandani A., Kumar HR, Alam SM, et.al. Prevalence of rgeumatic fever and rheumatic heart disease in rural and urban school children of district Kanpur(Abstr.).Indian Heart J 2000;52:192.
24. Jose V.J., Gomathi. Declining prevalence of rheumatic heart disease in rural school children in India 2001-2002. Indian Heart J 2003:55(2):158-60.
25. Mishra T.K.,Routray S.N., Satapathy C, et.al. Has the prevalence of rheumatic fever/ rheumatic heart disease really changed? A hospital-based study. Indian Heart J 2003:55(2):152-7.
26. Taranta A. A long term epidemiologic study of subsequent prophylaxis, streptococcal infections, and clinical sequlae: Relation of the rheumatic fever recurrence rate per streptococcal infection to the titres of streptococcal antibodies. Ann Intern Med 1964;60(Suppl.5):58.
27. Taranta A., Kleinberg E., Feinstein A, et al. A long term epidemiologic study of subsequent prophylaxis, streptococcal infections and clinical sequlae: Relation of the rheumatic fever recurrence rate per streptococcal infection to pre-existing clinical features of the patients. Ann Intern Med 1964;60(Suppl. 5):47.
28. Padmavati S. Rheumatic fever and rheumatic heart disease in developing countries. Bull WHO 978:56:543.

29. Zaman M.M. ,Rouf M.A. Haque S, et.al. Does rheumatic fever occur usually between the ages of 5 and 15 years? Int J Cardiol 1998;66:17-21.

30. Prukasakorn S, Sittisombut N. et. al. Epidemiological analysis of non M-typeable group A streptococcus isolates from a Thai population in northern Thailand. J Clin Microbiol 2000;38:1250-4.

31. Cunningham M.W. Autoimmunity and molecular mimicry in the pathogenesis of post-streptococcal heart disease. Front Biosci 2003;8:533-43.

32. Khanna A.K., Buskrik D.R., Williams RC, et.al. Presence of non HLA-B-Cell alloantigen in rheumatic fever patients and their families defined by monoclonal antibody. J Clin Invest 1989;83:1710 - 6.

33. Brock RC : The surgical and pathological anatomy of the mitral valve. Brit Heart J 1952; 14:489.

34. Rusted IE, Scheifley CH, Edwards JE: Studies of the mitral valve: II certain anatomic features of the mitral valve and associated structures in mitral stenosis. Circulation 1956;14:398

35. La Vecchia L, Zanolla L, Varotto L, et al. Reduced right ventricular ejection fraction as a marker for idiopathic dilated cardiomyopathy compared with ischemic left ventricular dysfunction. Am Heart J 2001;142:181–9.

36. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. J Am Coll Cardiol 1997;30:8–18.

37. Bunnell IL, Grant C, Greene DG. Left ventricular function derived from the pressure-volume diagram. Am J Med 1965;39:881–94.

38. Redington AN, Gray HH, Hodson ME, et al. Characterisation of the normal right ventricular pressure-volume relation by biplane angiography and simultaneous micromanometer pressure measurements. Br Heart J 1988;59:23–30.

39. Shaver JA, Nadolny RA, O'Toole JD, et al. Sound pressure correlates of the second heart sound. An intracardiac sound study. Circulation 1974;49:316–25.

40. Redington AN, Rigby ML, Shinebourne EA, et al. Changes in the pressure-volume relation of the right ventricle when its loading conditions are modified. Br Heart J 1990;63:45–9.

41. Weber KT, Janicki JS, Shroff S, et al. Contractile mechanics and interaction of the right and left ventricles. Am J Cardiol 1981;47:686–95.

42. Jardin F, Delorme G, Hardy A, et al. Reevaluation of hemodynamic consequences of positive pressure ventilation: emphasis on cyclic right ventricular afterloading by mechanical lung inflation. Anesthesiology 1990;72:966–70.

43. Cullen S, Shore D, Redington A. Characterization of right ventricular diastolic performance after complete repair of tetralogy of Fallot. Restrictive physiology predicts slow postoperative recovery. Circulation 1995;91:1782–9.

44. Sanchez-Quintana D, Anderson RH, Ho SY. Ventricular myoarchitecture in tetralogy of Fallot. Heart 1996;76:280–6.

45. Damiano RJ Jr, La Follette P Jr, Cox JL, et al. Significant left ventricular contribution to right ventricular systolic function. Am J Physiol 1991;261:H1514–24.

46. Hoffman D, Sisto D, Frater RW, et al. Left-to-right ventricular interaction with a noncontracting right ventricle. J Thorac Cardiovasc Surg 1994;107: 1496–502.

47. Brookes C, Ravn H, White P, et al. Acute right ventricular dilation in response to ischemia significantly impairs left ventricular systolic performance. Circulation 1999;100:761–7.

48. Penny DJ, Redington AN. Doppler echocardiographic evaluation of pulmonary blood flow after the Fontan operation: the role of the lungs. Br Heart J 1991;66:372–4.

49. Williams DB, Kiernan PD, Metke MP, et al. Hemodynamic response to positive end-expiratory pressure following right atrium-pulmonary artery bypass (Fontan procedure). J Thorac Cardiovasc Surg 1984;87:856–61.

50. Shekerdemian LS, Bush A, Lincoln C, et al. Cardiopulmonary interactions in healthy children and children after simple cardiac surgery: the effects of positive and negative pressure ventilation. Heart 1997;78:587–93.

51. Shekerdemian LS, Bush A, Shore DF, et al. Cardiorespiratory responses to negative pressure ventilation after tetralogy of Fallot repair: a hemodynamic tool for patients with a low-output state. J Am Coll Cardiol 1999;33:549–55.

52. D'Alonzo GE, Barst RJ, Ayres SM *et al*. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. *Ann Intern Med* 1991; **115:** 343–9.

53. Hinderliter AL, Willis PWt, Barst RJ *et al*. Effects of long-term infusion of prostacyclin (epoprostenol) on echocardiographic measures of right ventricular structure and function in primary pulmonary hypertension. Primary Pulmonary Hypertension Study Group. Circulation 1997; **95:** 1479–86.

54. Pinzani A.,Pinzani V.,et al. L insuffisance cardiaque droit pre et postoperatoire des mitraux et mitro-aortiques.Arch. Mal. Couer. 1993;86:27-34.

55. Hirata N.,Sakibara T,et al. Preoperative and postoperative right ventricular junction

during exercise in patients with mitral stenosis.J. Thorac. Cardiovasc. Surg.1992;104:1029-34.

56. Borer J S,Hochereiter C, Rosen S. Right ventricular function in severe non-ischemic mitral insufficiency. Eur Heart J 1991;12(Suppl. B):22-5

57. Groves P.H.,Lewis N.P.,et al. Reduced exercise capacity in patients with tricuspid regurgitation after successful mitral valve replacement for rheumatic mitral valve disease.Br. Heart. J. 1991;66:295-301.

58. White PA, BishopAJ, Conroy B, et al. The determination of volume of right ventricular casts using a conductance catheter. Eur Heart J 1995;16:1425–9.

59. White PA, Chaturvedi RR, Bishop AJ, et al. Does parallel conductance vary during systole in the human right ventricle? Cardiovasc Res 1996;32:901–8.

60. Chaturvedi RR, Kilner PJ, White PA, et al. Increased airway pressure and simulated branch pulmonary artery stenosis increase pulmonary regurgitation after repair of tetralogy of Fallot. Realtime analysis with a conductance catheter technique. Circulation 1997;95:643–9.

61. Brookes CI, White PA, BishopAJ, et al. Validation of a new intraoperative technique to evaluate loadindependent indices of right ventricular performance in patients undergoing cardiac operations. J Thorac Cardiovasc Surg 1998;116:468–76.

62. Jiang L, Siu SC, Handschumacher MD *et al*. Threedimensional echocardiography. In vivo validation for right ventricular volume and function. *Circulation* 1994; **89:** 2342–50.

63. Jiang L, Handschumacher MD, Hibberd MG *et al*. Threedimensional echocardiographic reconstruction of right ventricular volume: in vitro comparison with two-dimensional methods. *J Am Soc Echocardiogr* 1994; **7:** 150–8.

64. Levine RA, Gibson TC, Aretz T *et al*. Echocardiographic measurement of right ventricular volume. *Circulation* 1984; **69:** 497–505.

65. Geva T, Powell AJ, Crawford EC, et al. Evaluation of regional differences in right ventricular systolic function by acoustic quantification echocardiography and cine magnetic resonance imaging. *Circulation* 1998; **98:** 339– 45.

66. Kaul S,Tei C. Assessment of right ventricular function using two dimensional echocardiography. Am Heart J 1984;107:526-31.

67. Otto C M. Left and Right ventricular systolic function in Otto's Textbook of clinical Echocardiography, 3rd Edition, Page No.157

68. Sreedevi Gondi, Hisham Dokainish. Right ventricular tissue Doppler and strain imaging:Ready for clinical use? Echo. 2007;24(5):522-31

69. Alam M, Wardell J, Andersson E, et al. Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in healthy subjects. J. Am. Soc. Echocardiography 1999;12:618-28.

70. Lindquist P, Waldrenstorm A, et al: Regional and global right ventricular function in healthy individuals aged 20 – 90 years: A pulsed Doppler tissue imaging study. Echocardiography 2005;22:305-14.

71. Kukulski T.,Hubbert L., Arnold M, et al. Normal regional right ventricular function and its change with age: A Doppler myocardial imaging study. J. Am. Soc. Echocardiogr 2000;13:194-204.

72. Sundereswaran L., Nagueh S.F., Vardans et al. Estimation of left and right ventricular filling pressures after heart transplantation by tissue Doppler imaging. Am

J Cardiol 1998; 82:352-7

73. Torrent – Guast F, Ballester M, Buckberg GD, et al, Spatial orientation of the ventricular muscle band: Physiologic contribution and surgical implications. J Thorac Cardiovasc Surgery 2001;122:389 – 92.

74. Jamal E.,Bergerot C., Argaud L, et al. Longitudinal strain quantitates regional right ventricular contractile function. Am J Physiol Heart Circ Physiol 2003;285:H2842-7.

75. Dambrauskaite V., Herbots L.,et al. Differential changes in regional right ventricular function before and after a bilateral lung transplantation :an ultrasonic strain and strain rate study. J Am Soc Echo 2003;16:432-6.

76. Maceira A.,Prasad S.,et al. Reference right ventricular systolic and diastolic function normalized to age, gender, and body surface area from steady state free precession cardiac magnetic resonance. Eur Heart J 2006;27:2879-2888.

77. Mogelvang J.,Stubgaard M.,et al. Evaluation of right ventricular volumes measured by magnetic resonance imaging. Eur Heart J 1988;9:529-33.

78. Grothues F.,Maan J.C., et al. Interstudy reproducibility of right ventricular volumes,function,and mass with cardiovascular magnetic resonance. Am Heart J 2004;147:218-23.

79. Alfakih K.,Plein S.,et al. Comparision of right ventricular volume measurements between axial and short axis orientation using steady state free precession magnetic resonance imaging. J Magn Reson Imaging 2003;18:25-32.

80. Sato H.,Murakami Y., Shimada T, et al. Detection of right ventricular infarction by gadolinium DTPA-enhanced magnetic resonance imaging. Eur Heart J

1995;16:1195-9

81. Saba T.S.,Foster J.,Cockburn M, et al. Ventricular mass index using magnetic resonance imaging accurately estimates pulmonary artery pressure. Eur Respir J 2002;20:1519-24.

82. Roeleveld R.J., Marcus J.T., Boonstra A, et al. A comparision of non-invasive MRI-based methods of estimating pulmonary artery pressure in pulmonary hypertension. J Magn Resn Imaging 2005;22:67-72.

83. Wilkins M.,Paul G.,Strange J, et al. Sildenafil versus endothelin receptor antagonist for pulmonary arterial hypertension (SERAPH) study. Am J Respir Crit Care 2005;171:1199-1201.

84. Kuehne T.,Yilmaz S., Strendijk P, et al. Magnetic resonance imaging analysis of right ventricular pressure-volume loops: in vivo validation and clinical application in patients with pulmonary hypertension. Circulation 2004;110:2010-6.

85. Barst R.J., Langleben D., Frost A, et al. STRIDE-1 Study group.Sitaxsentan therapy for pulmonary arterial hypertension .Am J Respir Crit Care Med 2004;169:441-7.

86. Kurtulus Ozdemir,Bulent B., Gok H, et. al. Analysis of the myocardial velocities in patients with mitral stenosis. J Am Soc Echocardiography 2002;15:1472-8.

87. Mehta V.,Jamal Yusuf, Rastogi V, et.al. Acute effects of percutaneous mitral commissurotomy on right ventricular function in rheumatic mitral stenosis: A tissue Doppler echocardiographic study. Indian Heart J ;2003;9:84.

88. Saricam E, Ozbakir C, Pildrim N, et al. Evaluation of the relationship between functional capacity and right ventricular diastolic function in patients with isolated mitral stenosis and sinus rhythm:A tissue doppler study. Echocardiography

2007;24(2):134-9.

89. Alfred Bove,Frank James, Bove AA, James F, Wroblawski E, et. al. Right ventricular performance in mitral stenosis. Am J of Cardiol 1981;47:51-5.

90. Jonston DL, William Kostuk, Left and right ventricular function during symptom limited exercise in patients with isolated mitral stenosis .Chest 1986;89:186-90.

91. Cohen M.,Horowitz F.,et al. Response of the right ventricle to exercise in isolated mitral stenosis.Am J Cardiol. 1985;55:1054-8.

92. Gorlin R.,Sawyer C.G., Haeynes FW, et al. Effects of exercise on circulatory dynamics in mitral stenosis.III. Am Heart J 1950;29:192-203

93. Anthony P M, Claudia Goodwin. Exercise radionucloide angiography in patients with mitral stenosis:value of right ventricular response. Am H J 1986;112(3):509-17

94. The criteria committee for the New York Heart Association. Nomenclature and criteria for disease sixth edition. Little Brown and Company. 1964.

95. Sahn D.J.,Demaria A, Kisslo J, et al. The committee on M-mode standardisation of the American society of echocardiography.Recommendations regarding quantitation in M-mode echocardiography.Results of a survey of echocardiographic measurements. Circulation. 1978;58:1072-83.

96. Schiller N.B.,Shah P.M., Crawford M, et al. Recommendations for quantitation of the left ventricle by two dimensional echocardiography.J.Am.Soc. Echocardiography 1989;2:358-67.

97. Hatle L.,Anglesen B.A., Tromsdal A, et al. Non-invasive assessment of atrioventricular pressure half time by Doppler ultrasound. Circulation.1979;60:1096-1101.

98. Rowe J.C.,Bland E.F., Spraque HB, et al. The course of mitral stenosis without surgery: Ten and twenty year perspectives. Ann Intern Med 1960;52:741-9.

99. Ozdemir K, Altunkeser BB, Gok H , et al.:Analysis of the myocardial velocities in patients with mitral stenosis. J Am Soc Echocardiogr 2002;15(12);1472-8.

100. Clyne C A , Alpert J S ,Benotti J R :Interdependence of the left and right ventricles in health and disease. Am Heart J 1989;117:1366-73.

101. Cicala S , Galderisi M ,Caso P, et al. Right ventricular diastolic dysfunction in arterial systemic hypertension:Analysis by pulsed tissue Doppler. Eur J Echocardiogr 2002;3:135-42.

PROFORMA

RV Diastolic Function in Mitral Stenosis

Sl No. : Name : Hosp. No.
Age/Sex:

Previous CMV : Yes / No Date : (month / year)

Previous BMV : Yes / No Date (month / year)

Duration of symptoms : Years Months

Symptoms class NYHA :

PET level ground :

PET Stairs :

ECG :

ECHO : LVEF : LA size (PSLAX) mm

Mitral valve score (total): Thickness :

Subvalvar: Mobility: Calcification

MR grade : Nil / mild / moderate / severe RJA / LAA (sq.cm) :

TR grade : Nil / mild / moderate / severe AR grade : Nil / mild / moderate / severe

Other lesions: AS / TS severity:

Thrombus in the left atrium (location and size)

Doppler MVO cm^2 1. 2. 3.

2D MVO cm^2 1. 2. 3.

RV function

EDV : ESV: EF :

S wave (vel, m/sec) IVCT (msec) RV Ejection time:

E’ : A’ : E’/A’ : IVRT : Tei Index:

GLOSSARY FOR THE MASTER SHEET

ID - Identification

Hosp - Hospital Number

Sex - Male :1, Female :2

BMV - Balloon mitral valvotomy / closed mitral valvotomy done = 1, not done = 2

Class - New York Heart Association class from 1 to 3

ECG - Electrocardiogram

LA - Left atrial size

LVEF - Left Ventricular Ejection Fraction

Score - Mitral valve score

MR - Mitral regurgitation, 1 = trivial 2 = mild

TR - Tricuspid regurgitation, 1 = trivial, 2 = mild

Gdt - Tricuspid regurgitation gradient

Dop - Doppler derived mitral valve area

MVA - Mitral valve area (planimetry)

Gra - Gradient across mitral valve

EDV - End diastolic volume (Right ventricular)

ESV - End systolic volume (Right ventricular)

RVEF - Right ventricular ejection fraction

S - S wave velocity

Ea - E'wave velocity (Right ventricular Tissue Doppler)

Aa - A' wave velocity (Right ventricular tissue doppler)

E Aa - E'/A' ratio

IVCT - Isovolumic contraction time

IVRT - Isovolumic relaxation time

ET - Ejection time

TI - Tei Index